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HUMAN CONVALESCENT SERUM IN THE TREATMENT OF PREPARALYTIC POLIOMYELITIS

A COMPARISON OF 447 TREATED AND 102 CONTROL PATIENTS IN NEW YORK CITY IN 1931

ALFRED E. FISCHER, M.D.

NEW YORK

The personal equation often makes a statistical study of a clinical problem in medicine difficult. Much discrimination is needed in order to obtain two strictly comparable groups of patients in order that one of them may be used as a control. Proper precautions must be taken in advance in collecting data in order to prevent the results from being obscured by variables which may make the study useless.

Having these facts in mind, the Poliomyelitis Committee of the New York Academy of Medicine attempted to estimate the value of convalescent human poliomyelitis serum [1] the efficacy of which had been established on the basis of Flexner and Lewis' [2] studies on experimental animals. Unfortunately, earlier work on human beings [3] had been done without proper control cases, and, with few exceptions, paralytic as well as preparalytic patients were treated. Later it became obvious that the disease in the paralytic stage was already too far advanced to test the therapeutic value of the serum, so the tendency in the last ten years has been to restrict the use of serum to patients in the early stage of the disease before paralysis occurs.

The patients included in this analysis were seen during July, August, September and October 1931. In this time 4,046 cases of poliomyelitis

This study was made under the auspices of the New York Academy of Medicine, Dr. Linsly R. Williams, Director, and was aided by a grant from the Rockefeller Institute for Medical Research.

1. A preliminary report of this work by L. R. Williams appeared in the Bulletin of the New York Academy of Medicine (**8**:613 [Oct.] 1932). Some earlier work (1927-1930) was recorded in that paper, together with a detailed description of the method used in the preparation of the convalescent serum and a list of instructions for the use of the physicians who cooperated with the Poliomyelitis Committee.

2. Flexner, S., and Lewis, P. A.: Experimental Poliomyelitis in Monkeys, J. A. M. A. **54**:1780 (May 28) 1910.

3. Aycock, W. L., and Luther, E. H.: Preparalytic Poliomyelitis: Observations in One Hundred and Six Cases in which Convalescent Serum was Used, J. A. M. A. **91**:387 (Aug. 11) 1928.

were reported in New York City. The group of physicians [4] acting as consultants for the Academy of Medicine examined approximately 800 patients. About 200 of these were seen after paralysis had set in; 579, during the preparalytic stage. These 579 patients formed the basis of the present study. In spite of a predetermined plan,[1] the study could unfortunately not be carried out exactly as intended. It had been decided to treat alternate patients, using every other patient as a control. However, it became a practical impossibility to treat only alternate patients because the family physician, with whom most patients were seen, usually requested that serum be used, and as a result, many more patients were treated than not. A large number of controls were obtained only because there were days during the epidemic when insufficient serum was available, and consequently many patients who could not be treated automatically became controls. In this way there were 102 patients in whose cases the diagnosis was made but who were not treated, while the remaining 477 patients received serum.

The preparalytic stage of the disease has been known since Wickman [5] called attention to it in 1907. Although many writers still question the possibility of detecting early cases, it may be said that more persons in the preparalytic stage presented themselves for treatment in 1931 because of early diagnosis rather than because there were more cases of this type in New York City in 1931 than in previous epidemics. That so many early cases were seen was due in part to the fact that this was the first large epidemic that has occurred since the radio has become so integral a part of American home life. Newspapers, in addition, stressed the symptomatology of the disease, and because of the widespread concern and the authentic information that was distributed through various channels, every one became so familiar with the early signs of the disease that many lay persons actually made the diagnosis before a physician was called or paralysis occurred.

The symptomatology presented by the patients with preparalytic poliomyelitis whom we saw did not vary greatly from that described in earlier epidemics.[6] As a matter of fact, these patients are more accurately classified not as preparalytic but as meningitic, for the term

4. Drs. Jacques M. Lewis, Harry S. Mackler, Sidney D. Leader, William E. Messer, Carl H. Smith, Stanley S. Lamm, Harry S. Lichtman, David Merksamer and Milton E. Robbins assisted me in examining and treating the patients analyzed in this report. Dr. Alice Paulsen of the New York Academy of Medicine made the tables and offered many valuable suggestions in the preparation of the paper.

5. Wickman, I.: Beiträge zur Kenntnis der Heine-Medinschen Krankheit, Berlin, S. Karger, 1907.

6. Peabody, F. W.; Draper, G., and Dochez, A. R.: A Clinical Study of Acute Poliomyelitis, New York, Rockefeller Institute for Medical Research, 1912, Monograph 4. Aycock and Luther.[3]

"preparalytic" infers that they would have become paralyzed had they not been treated with serum. Although "meningitic" is the preferable term, the patients will be called "preparalytic" to avoid misunderstanding. The diagnosis for each of our 579 preparalytic patients was made on the basis of the history, clinical course, physical findings and pathologic changes in the spinal fluid. Lumbar punctures were done at the bedside, and the fluid was examined microscopically and chemically in most instances immediately following its removal. A great many of the patients with preparalytic poliomyelitis were seen on the first or second day following the onset of constitutional symptoms, but many more were seen after signs of cerebral or meningeal irritation had appeared. The diagnostic criteria were the same for the treated as for the control group. A number of other conditions were encountered, but these were excluded by means of lumbar puncture. Most of our preparalytic patients were examined in bed. We did not think it advisable to place a patient in the early stage of the disease on the floor for detailed muscle tests. It is, moreover, sometimes difficult in the presence of tremors to state whether or not a muscle is beginning to show evidence of paralysis. Since at least 73 per cent of our patients showed no paralysis after three weeks of illness, it seems safe to state that at least that many did not have any paralysis when they were first examined. It is, therefore, unlikely that we missed any but the slightest paralysis on our initial examination. Accurate data were recorded at the time of the first examination, the following day, three weeks after the onset and after from five to six months. The data were subsequently analyzed and comparisons made between the treated and the untreated patients.

In classifying the patients with reference to their condition at the onset and on discharge, we used the following symbols: 0 indicates no paralysis; ±, weakness equivalent to slight paralysis; +, moderate paralysis of a muscle group in one extremity; + +, definite paralysis of muscle groups of two extremities or two sets of muscle groups, and + + +, severe paralysis involving muscle groups of three extremities or of two extremities and the trunk.

We did not attempt to estimate mathematically the amount of paralysis, as Aycock and Luther [3] did. The groupings which we have indicated gave us a fairly accurate picture of the extent of muscle involvement in our large series. Each patient whose condition we have classified as 0 both at the beginning of the illness and at the time of the final examination was completely examined in bed at the onset and out of bed at the termination of the illness. In only three instances were patients paralyzed at the time of the final visit for whom a rating of 0 had been recorded three weeks after the onset. We may therefore be fairly certain that our examination in bed was accurate enough to yield a minimal error in the final analysis.

With this classification of the degree of paralysis in mind, one may now proceed to a consideration of the details of the various aspects of our study.

Because of the lack of agreement as to the prognostic significance of any one physical finding in the initial stage of the disease, it is difficult to determine which facts are likely to yield results in a statistical analysis designed to bring out possible relationships between the condition at the beginning of treatment and the outcome. We therefore considered some of these variants in order to determine if possible their importance as factors in the incidence and outcome of the disease.

SEX

McAusland [7] stated that in most epidemics there has been a slightly higher incidence among males as compared with females. This fact we have substantiated in the present study. There were 57 per cent males and 43 per cent females in the treated group and 62.7 per cent males and 37.3 per cent females in the untreated group. The evidence, however, is not conclusive as to whether the outcome of the disease is more disastrous in males than in females. In both groups a slightly smaller proportion of the females escaped without paralysis (0), but in the treated group a slightly higher percentage of females showed the more serious residual effects (+ + and + + +). On the other hand, in the untreated group the males showed a slightly higher percentage of these degrees of paralysis. The differences are so slight that definite conclusions cannot be drawn.

AGE

Studies of susceptibility at different ages during most of the recorded epidemics have shown that the period of greatest susceptibility was the second year of life and that after the fifth year the susceptibility declined. In rural districts the age of those affected has been higher than in urban districts.[8] The greatest number of patients in our series were in the third year of life (15.3 per cent of the treated and 17.7 per cent of the untreated group). Approximately 50 per cent of each group were 5 years of age or under. There was a marked decline in susceptibility after the sixth year. The percentage of cases then runs parallel in each group for each year from the seventh to the fifteenth. None of the untreated patients was over 14 years of age, while 6.4 per cent of the treated patients were 15 or over. The untreated patients on the whole were slightly younger than the treated patients.

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7. McAusland, W. R.: Poliomyelitis, Philadelphia, Lea & Febiger, 1927, p. 38.

8. Shaw, H. L. K.: Results of the Recent Epidemic of Poliomyelitis in New York State, J. A. M. A. **69**:166 (July 21) 1917. Aycock, W. L.: A Study of the Significance of Geographic and Seasonal Variations in the Incidence of Poliomyelitis, J. Prev. Med. **3**:245 (May) 1929.

In 1916, Nicoll [9] showed that the greatest number of fatalities in the New York State epidemic occurred among infants under 1 year of age and among persons over 15. Tables 1 and 2 show the age distribution of the two groups in our series studied in relation to outcome. Three

TABLE 1.—*Age and Outcome for the Treated Group*

	Degree of Paralysis							
Age, Years	0	±	+	++	+++	Died	Total	Per Cent
1	8	1	0	0	0	0	9	1.9
2	24	2	3	1	0	0	30	6.3
3	52	3	12	4	0	2	73	15.3
4	42	0	7	5	6	3	63	13.2
5	38	11	4	6	4	2	65	13.6
6	40	3	2	2	1	1	49	10.3
7	29	3	4	0	1	2	39	8.2
8	20	3	1	4	1	0	29	6.1
9	18	4	1	2	1	3	29	6.1
10	16	1	2	1	2	2	24	5.0
11	8	2	3	0	0	0	13	2.7
12	5	1	1	0	1	1	9	1.9
13	8	1	1	2	0	1	13	2.7
14	3	0	1	1	0	0	5	1.1
15	3	0	0	0	1	0	4	0.8
16	0	0	0	1	0	0	1	0.2
Over 16	15	1	2	2	1	1	22	4.6
Total	329	36	44	31	19	18	477	100.0
Per cent of patients	69.0	7.5	9.2	6.5	4.0	3.8	100.0	

Average age, 6.5

TABLE 2.—*Age and Outcome for the Control Group*

	Degree of Paralysis							
Age, Years	0	±	+	++	+++	Died	Total	Per Cent
1	2	1	..	1	..	..	4	3.9
2	11	..	2	..	..	1	14	13.7
3	12	3	1	2	..	..	18	17.7
4	12	1	..	..	1	..	14	13.7
5	8	1	..	1	..	..	10	9.8
6	8	1	1	..	1	..	11	10.8
7	5	2	..	..	..	..	7	6.9
8	4	..	1	..	..	..	5	4.9
9	1	..	1	..	1	1	4	3.9
10	4	..	..	..	..	..	4	3.9
11	3	1	..	..	..	..	4	3.9
12	1	..	..	..	..	..	1	1.0
13	..	2	1	..	1	..	4	3.9
14	1	..	..	1	..	..	2	2.0
15	..	..	..	..	..	..	..	....
16	..	..	..	..	..	..	..	....
Over 16	..	..	..	..	..	..	..	....
Total	72	12	7	5	4	2	102	100.0

Average age, 5.2

deaths occurred in the fourth and three in the ninth year group. In spite of the fact that there were 477 patients, when this number is divided into the various age levels, the number of each age becomes small. As a result, it cannot be said that the data are conclusive as regards the relation of age to seriousness of outcome.

9. Nicoll, M. Jr.: Epidemiologic Data in the Poliomyelitis Epidemic in New York State, Tr. Am. Pediat. Soc. **29**:228, 1917.

TEMPERATURE

The temperature and the outcome for both the treated and the untreated group are shown in tables 3 and 4. The temperature recorded is that at the time of examination or the highest temperature previously recorded. A considerable number of patients were seen on the first day of the illness, and therefore their records probably indicate the highest temperatures at the onset of the disease. Many others, however, were

TABLE 3.—*Temperature in Relation to Outcome for the Treated Group*

	Degree of Paralysis												Died		Total	
	0		±		+		++		+++							
Temperature, F.	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent			No.	Per Cent	No.	Per Cent
100 or less	31	9.4	1	2.8	2	4.5	1	3.2	0	0.0			1	5.6	36	7.6
101 or less	88	26.8	13	36.1	11	25.0	7	22.6	4	21.0			2	11.1	125	26.2
102 or less	118	35.9	7	19.4	21	47.7	13	41.9	8	42.1			6	33.3	173	36.2
103 or less	56	17.0	10	27.8	9	20.5	7	22.6	6	31.6			4	22.2	92	19.3
104 or less	29	8.8	5	13.9	1	2.3	3	9.7	1	5.3			4	22.2	43	9.0
105 or less	7	2.1	0	0.0	0	0.0	0	0.0	0	0.0			1	5.6	8	1.7
Total.....	329		36		44		31		19				18		477	

TABLE 4.—*Temperature and Outcome for the Control Group*

	Degree of Paralysis							
Temperature, F.	0	±	+	++	+++	Died	Total	Per Cent of Group
100 or less.....	2	3	1	1§	0	0	7	6.9
101 or less.....	16*	1	3	4§	0	0	24	23.5
102 or less.....	42†	3	1	0	4‖	1	51	50.0
103 or less.....	5	3	2	0	0	0	10	9.8
104 or less.....	7	2	0	0	0	1	10	9.8
Total.....	72‡	12	7	5	0	2	102	100.0

* Including four patients for whom the degree of fever was designated as "mild," the temperature not being given exactly.

† Including fifteen patients for whom the degree of fever was designated as "moderate," the temperature not being given exactly.

‡ Including two patients for whom the degree of fever was designated as "high," the temperature not being given exactly.

§ Patients for whom the degree of fever was designated as "mild" and "moderate," the temperature not being given exactly.

‖ Including two patients for whom the degree of fever was designated as "moderate," the temperature not being given exactly.

not seen immediately, and it is possible that higher temperatures than those recorded may have been present earlier in the illness. Table 5 shows that there may be a relationship between the outcome and comparatively low temperature, on the one hand, and comparatively high temperature, on the other. For, of the patients in the treated group having no residual effects, 36.2 per cent had a temperature of 101 F. or under (table 3), while only 10.9 per cent had a temperature above 104 F. Among those who died, only 16.7 per cent had a temperature of 101 F. or under, while 27.8 per cent had a temperature above 103 F. As shown in table 5, 86.1 per cent of the patients with a temperature of 100 F. or under recovered without residual effects, while only 2.8 per cent of

them died, while 70.4 per cent of the patients with a temperature 101 F. or under had no residual effects and only 1.6 per cent of them died. At the other extreme, only 67.5 per cent of those with a temperature of from 103 to 104 F. at the onset escaped without some paralysis, and 9.3 per cent of these patients died. One of the 8 patients whose initial temperature was over 104 F. died. There were 51 patients in all with a temperature of over 103 F. at the onset. Five of these patients died, approximately 10 per cent. Since these patients were all seen in the preparalytic stage, it is fair to conclude that the higher temperatures are evidence of potential bulbar involvement. It is well known that patients with bulbar symptoms, particularly those in whom the disease terminates fatally, frequently have very high temperatures. It will subsequently be shown that the recorded temperatures are of further importance in that they form one basis for comparing the severity of cases.

TABLE 5.—*Outcome in Relation to Temperature for the Treated Group*

	Degree of Paralysis							
	0	±	+	++	+++	Died,	Total Patients	
Temperature	Per Cent of Patients	Per Cent of Patients	Per Cent of Patients	Per Cent of Patients	Per Cent of Patients	Per Cent of Patients	No.	Per Cent
100 or less	86.1	2.8	5.5	2.8	0.0	2.8	36	100
101 or less	70.4	10.4	8.8	5.6	3.2	1.6	125	100
102 or less	68.2	4.1	12.1	7.5	4.6	3.5	173	100
103 or less	60.9	10.9	9.8	7.6	6.5	4.3	92	100
104 or less	67.5	11.6	2.3	7.0	2.3	9.3	43	100
105 or less	87.5	0.0	0.0	0.0	0.0	12.5	8	100

We have not been impressed by the statement that the course of the temperature can be taken as a guide for treatment,[10] for the temperature in poliomyelitis usually falls on the third or fourth day following the onset of signs of involvement of the nervous system, irrespective of treatment. On the other hand, the temperature sometimes rises for thirty-six hours following intraspinal and intravenous or intramuscular injections of serum, even though the infectious process may at the same time have subsided. In some cases with bulbar symptoms the temperature may again rise after having been normal for three or four days.

SPINAL FLUID CELL COUNT

The data with regard to the spinal fluid cell count were also subjected to analysis with a view to determining statistically whether any relationship could be demonstrated between this factor and the end-

10. MacNamara, J., and Morgan, F. G.: Poliomyelo-Encephalitis: Treatment by Human Immune Serum, Lancet **1**:469 (Feb. 27) 1932.

result. There is a suggestion that a very low cell count tends to favor a good prognosis, and a very high cell count, a poor one. Of the treated patients having 50 or less cells per cubic centimeter, 78 per cent escaped residual effects and none died, whereas of the group of twenty-seven having over 500 cells, only 40.8 per cent showed no residual effects and 22.2 per cent died. In addition, 19.7 per cent of the patients who escaped residual paralysis showed counts of less than 50 cells, and 24 per cent, counts of less than 100, whereas only 3.4 per cent of those with counts of more than 500 cells escaped paralysis. Of those who died, none had less than 50 cells, whereas 35.2 per cent of those who died had over 500 cells.[11] Hunt [12] recently stated that the patients with fatal cases in his series had an average count of over 200 cells.

In our control group, 53 patients, or 52 per cent, had less than 100 cells, as compared to 190 patients, or 40.5 per cent, of the treated group. At the other extreme, 5 patients, or 4.9 per cent, of the control group had counts of over 500 cells, as against 27, or 5.8 per cent, of 477 patients in the treated group. There was, therefore, a greater percentage of patients with less than 100 cells and a smaller percentage having more than 500 cells in the control group. Moreover, the largest percentage of patients who showed the severest grade of paralysis (+ + +) both in the treated and in the control group occurred among those who had more than 500 cells.

One must remember that the spinal fluid cell count may vary from day to day. Eighty-two, or 17.5 per cent, of our treated preparalytic patients had counts of less than 50 cells. However, many of these patients were seen on the first day of the disease, and it is possible that they would have had a higher cell count had the fluid been examined a second time. Daily counts were made in some cases. These frequently showed fluctuations of as many as 50 cells on subsequent days, the tendency being to a fall after the fifth day with a disappearance of cells by the seventh or eighth day of the disease. There were 2 patients among approximately 800 in whose spinal fluid no cells were observed when the patient was first seen. In 1 instance, although poliomyelitis was suspected, cells did not appear in the spinal fluid until the fourth day of the illness, at which time 110 cells were counted. Concomitantly paralysis of one extremity was noted. In the other patient cells appeared on the day following the first negative puncture. Levinson [13] recently reported several similar instances.

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11. Eighteen patients in all died. Unfortunately, a cell count was not made for 1 patient, and this patient has been excluded in the calculations.

12. Hunt, L. W.: A Clinical Study of Epidemic Poliomyelitis, Am. J. Dis. Child. **44**:1377 (Dec.) 1932.

13. Levinson, S. O.: Early Acute Anterior Poliomyelitis Without Increase of Cells in the Spinal Fluid, J. Pediat. **1**:337 (Sept.) 1932.

DIFFERENTIAL SPINAL FLUID CELL COUNT

Whereas the actual number of cells was carefully counted at the bedside, it was not possible to examine smears and make differential counts in every case. As Thelander, Shaw and Limper [14] have pointed out, the examination of the stained smear of spinal fluid is often a hazardous undertaking. Not only is the type of white cell often confused by shrinkage in fixing and staining, but red cells, which would have been excluded in doing a cell count, frequently are mistaken for lymphocytes on a stained smear. We did not endeavor to corroborate Thelander, Shaw and Limper's statement that the type of cell which is present in a given case persists throughout the illness. However, we confirmed their work [14] in those cases in which we made a reexamination. The earlier conception of an initial polymorphonuclear pleocytosis which changes to a mononuclear one is probably incorrect, for in the spinal fluid of many of the preparalytic patients whom we examined on the first day of illness we found a predominance of mononuclear cells. We have, however, insufficient data on which to base definite conclusions concerning differential smears.

STAGE OF EPIDEMIC

It has been stated [15] that the more severe cases occur in the beginning and middle of an epidemic and the milder cases at the end. We studied the monthly variation in the incidence and outcome for the treated and the control patients. In the largest number of patients in each series the onset occurred during August, and about the same percentage in the two groups were seen during the other three months of the epidemic. The data which we tabulated do not yield conclusive evidence as to the relative virulence of the disease at various stages of the epidemic. For example, the same proportion of treated patients recovered among those whose illness began in August and among those with the onset in October (72.4 as compared to 72.6 per cent). In addition, approximately the same percentage of treated patients died among those seen during each of the first three months (3.8 per cent of those seen in July, 4.4 per cent of those seen in August and 3.4 per cent of those seen in September). None of the 21 patients observed in October died, but this was the smallest group. The only 2 deaths in the control group occurred during September. The data suggest that the virulence does not vary at different stages of the epidemic. In the New York City epidemic of 1916 [16] the ratio of deaths to cases was between 26 and 30

14. Thelander, H. E.; Shaw, E. B., and Limper, M. A.: The Spinal Fluid Cytology in Poliomyelitis: A Graphic Study, Am. J. Dis. Child. **42**:1117 (Nov.) 1931.

15. Kellogg, W. H.: The Present Status of Convalescent Serum Therapy, J. A. M. A. **93**:1927 (Dec. 21) 1929.

16. Epidemic of Poliomyelitis in New York, 1916, New York City, Department of Health, 1917, p. 105.

per cent in each month. This again demonstrates that there is no marked change in the virulence throughout an epidemic of poliomyelitis.

DAY OF TREATMENT

Advocates of serum therapy urge its early administration. Tables 6 and 7 show the number of serum-treated patients tabulated with reference to the outcome and the day of treatment, calculated both from the day of onset of the illness and from the date of the first appearance of meningeal symptoms. In some instances there was the "latent period," and in others the first meningeal symptoms occurred soon

TABLE 6.—*Day of Treatment and Outcome for Treated Group*

Day of Treatment*	Degree of Paralysis					Died	Total	Per Cent
	0	±	+	++	+++			
1 Onset of disease	43	3	6	3	0	1	56	11.8
Onset of meningeal symptoms	186	15	16	17	11	7	252	52.8
2 Onset of disease	116	7	14	14	5	5	161	33.9
Onset of meningeal symptoms	100	13	21	13	6	8	161	33.8
3 Onset of disease	71	10	9	6	7	7	110	23.2
Onset of meningeal symptoms	24	5	4	1	1	1	36	7.5
4 Onset of disease	40	7	10	5	3	3	68	14.3
Onset of meningeal symptoms	11	2	2	0	1	0	16	3.4
5 Onset of disease	22	4	1	2	3	1	33	6.9
Onset of meningeal symptoms	2	0	0	0	0	0	2	0.4
6 Onset of disease	13	1	3	1	1	1	20	4.2
Onset of meningeal symptoms	1	1	0	0	0	0	2	0.4
7 Onset of disease	6	1	0	0	0	0	7	1.5
Onset of meningeal symptoms	0	0	0	0	0	0	0	0.0
After 7 days from onset of disease	16	3	1	0	0	0	20	4.2
After 7 days from onset of meningeal symptoms	0	0	0	0	0	0	0	0.0
Before onset of disease	0	0	0	0	0	0	0	0.0
Before onset of meningeal symptoms	5	0	1	0	0	2	8	1.7
Time of onset not stated	2	0	0	0	0	0	2	
Total onset data	327	36	44	31	19	18	475	100.0
Total meningeal symptoms data	329	36	44	31	19	18	477	100.0

* Average, third day from onset of illness.

after the onset of the illness. The greatest number of the patients whom we treated with convalescent serum received their first dose on the second day of illness and on the first day of meningeal symptoms. The average time of treatment for the whole group was the third day of illness, or about the middle of the second day from the onset of meningeal symptoms. In the control group, while the greatest number of patients were first seen on the third day of illness and on the first day of their meningeal symptoms, the average time was about the middle of the fourth day from the onset of the illness and the second day of meningeal symptoms, slightly later than the treated group. The significance of the difference in the duration of the cases when the patients were first seen will be discussed subsequently.

Table 8 shows the outcome for patients treated on various days after the onset of the disease. The highest percentage of deaths occurred among those who received serum on the third day; the lowest, among

TABLE 7.—*Day of Examination and Outcome for Control Group*

Day of Examination*	Degree of Paralysis 0	±	+	++	+++	Died	Total	Per Cent
1 Onset of disease	8	3	0	2	0	1	14	13.7
Onset of meningeal symptoms	30	4	1	4	1	2	42	41.2
2 Onset of disease	16	..	1	2	1	..	20	19.6
Onset of meningeal symptoms	17	4	3	..	3	..	27	26.4
3 Onset of disease	17	2	..	0	2	..	21	20.6
Onset of meningeal symptoms	15	2	2	1	0	..	20	19.6
4 Onset of disease	11	1	3	1	1	..	17	16.7
Onset of meningeal symptoms	2	..	..	..	0	..	2	2.0
5 Onset of disease	10	2	1	..	..	1	14	13.7
Onset of meningeal symptoms	1	1	..	..	..	..	2	2.0
6 Onset of disease	4	1	1	..	..	..	6	5.9
Onset of meningeal symptoms	0	1	..	..	..	..	1	1.0
7 Onset of disease	3	..	1	..	..	..	4	3.9
Onset of meningeal symptoms	0	..	..	..	..	..	..	...
After 7 days from onset of disease	2	3	..	..	..	..	5	4.9
After 7 days from onset of meningeal symptoms	0	..	..	..	..	..	..	...
Date of onset of disease not known	1	..	..	..	..	..	1	1.0
Date of onset of meningeal symptoms not known	5	..	..	..	..	..	5	4.9
Before onset of meningeal symptoms	2	..	1	..	..	..	3	2.9
Total onset data	72	12	7	5	4	2	102	100.0
Total meningeal symptom data	72	12	7	5	4	2	102	100.0

* Average day of examination calculated from onset of disease, 3.5; average calculated from onset of meningeal symptoms, 2 (exclusive of those treated before the onset of meningeal symptoms).

TABLE 8.—*Outcome According to Day of Treatment Calculated from Onset of Disease*

Days	Degree of Paralysis 0 Per Cent of Patients	± Per Cent of Patients	+ Per Cent of Patients	++ Per Cent of Patients	+++ Per Cent of Patients	Died, Per Cent of Patients	Total Patients No.	Per Cent
1	76.7	5.4	10.7	5.4	0.0	1.8	56	100
2	72.0	4.4	8.7	8.7	3.1	3.1	161	100
3	64.5	9.1	8.2	5.4	6.4	6.4	110	100
4	58.8	10.3	14.7	7.4	4.4	4.4	68	100
5	66.7	12.1	3.0	6.1	9.1	3.0	33	100
6	65.0	5.0	15.0	5.0	5.0	5.0	20	100
7	85.7	14.3	0.0	0.0	0.0	0.0	7	100
After 7	80.0	15.0	5.0	0.0	0.0	0.0	20	100

those treated on the first day and on the seventh day or later. The number of patients composing these two groups was too small, however, to make a comparison valid. The low mortality for the patients treated on the first day of the preparalytic stage of the disease may be explained by the clinical fact that poliomyelitis is rarely fatal within twenty-four hours of the onset of the disease. On the other hand, most patients

who have survived seven days of illness without paralysis have passed through the stage of their illness when paralysis would probably have occurred.

DOSAGE

By far the greatest number of patients (364, or 76.3 per cent) received two doses of serum, while 113, or 23.7 per cent, received only one dose. The difference in outcome in respect to the number of treatments was not significant.

As shown by table 9, most of the patients (68.6 per cent) received between 70 and 80 cc. of serum. The numbers of patients given the other doses is so small that it is not possible to calculate a correlation between dosage and outcome, presuming that such a relationship may exist.

TABLE 9.—*Outcome and Amount of Serum Administered*

Amount, Cc.*	Degree of Paralysis					Died	Total	Per Cent
	0	±	+	++	+++			
40 or less	49	10	0	0	2	4	65	13.6
41 to 50	1	0	6	3	0	1	11	2.3
51 to 60	13	1	3	3	1	3	24	5.1
61 to 70	3	3	2	0	0	0	8	1.7
71 to 80	236	20	26	24	14	7	327	68.6
81 to 90	6	0	1	0	0	1	8	1.6
91 to 100	14	1	2	1	2	2	22	4.6
101 to 110	7	1	1	0	..	..	9	1.9
111 to 120	..	..	..	..	..	..	..	....
121 to 130	..	..	..	..	..	..	..	....
131 to 140	..	..	..	..	..	..	..	....
141 to 150	..	..	2	..	..	..	2	0.4
151 to 160	..	..	1	..	..	..	1	0.2
Total	329	36	44	31	19	18	477	100.0

* Average, 75 cc.

METHOD OF ADMINISTRATION OF SERUM

The results of treatment of preparalytic or paralytic poliomyelitis by different methods of administration of serum have been discussed by many writers. Most of the results, particularly in the preparalytic stage, have been good no matter which method has been used. For example, McEachern and Bell,[17] Lomer and Shirreff [18] and Hardman and McKay [19] showed excellent results when only from 25 to 30 cc. of serum was given intramuscularly, while Shaw, Thelander and Fleischner [20] and

17. McEachern, J. M., and Bell, L. G.: Lessons from Poliomyelitis Epidemic in Manitoba, Canad. Pub. Health J. **20**:427 (Sept.) 1929.

18. Lomer, T. A., and Shirreff, U. T.: Report of an Epidemic of Poliomyelitis in Ottawa, 1929, Canad. Pub. Health J. **21**:53 (Feb.) 1930.

19. Hardman, R. P., and McKay, A. L.: Poliomyelitis in Ontario, Canad. Pub. Health J. **21**:77 (Feb.) 1930.

20. Shaw, E. B.; Thelander, H. E. and Fleischner, E. C.: Convalescent Serum in Preparalytic Cases of Poliomyelitis: Results of Intramuscular Administration, J. A. M. A. **85**:1555 (Nov. 14) 1925.

Shaw, Thelander and Limper [21] have used larger doses intramuscularly. The earliest workers, Zingher,[22] Netter [23] and Schwarz [24] used the intraspinal method alone. In more recent epidemics patients have been treated by combining the intraspinal and intramuscular or the intraspinal and intravenous methods.[6] No attempt has ever been made to compare one type of treatment with another in the same epidemic. This is an important point, for the virulence of cases in different epidemics may vary. It is manifestly unfair to compare the results of one method of serum administration in one epidemic with the results of another method in another locality in a different year. We were fortunate in this regard to have treated a considerable number of patients by each method. Unfortunately, the same number of patients were not treated by each method, nor was it possible to say whether the more serious cases were

TABLE 10.—*Outcome and Technic of Administration of Serum*

Method	Degree of Paralysis					Died, Per Cent of Patients	Total Patients	
	0 Per Cent of Patients	± Per Cent of Patients	+ Per Cent of Patients	++ Per Cent of Patients	+++ Per Cent of Patients		No.	Per Cent
Intraspinal	....	....	....	...	...	...	..	...
Intravenous	66.7	0.0	33.3	0.0	0.0	0.0	6	100
Intramuscular	61.9	16.6	8.3	6.0	1.2	6.0	84	100
Intraspinal-intravenous	70.0	6.7	6.7	4.4	7.8	4.4	90	100
Intraspinal-intramuscular	71.2	5.4	9.3	7.3	4.4	2.4	205	100
Intravenous-intramuscular	69.8	6.4	9.5	6.4	3.2	4.7	63	100
Intraspinal-intravenous-intramuscular	69.0	3.4	13.8	10.4	0.0	3.4	29	100

in one group or in the other. Nearly every one of our patients received serum immediately on withdrawal of spinal fluid. In only a few instances was there a delay between the diagnostic puncture and the onset of therapy, and the delay in these cases cannot have been significant. As indicated in table 10 the majority of our patients were treated by the combined intraspinal and intramuscular administration of serum, 205, or 43 per cent, being treated in this way and 84, or 17.6 per cent, by the intramuscular method alone.

The question as to whether the intraspinal route is preferable or whether it does harm, as has been claimed, can best be answered by a comparison of the results of treatment. The majority of patients (324,

21. Shaw, E. B.; Thelander, H. E., and Limper, M. A.: Treatment of Poliomyelitis, J. A. M. A. **97**:1620 (Nov. 28) 1931.

22. Zingher, A.: The Diagnosis and Serum Treatment of Anterior Poliomyelitis, J. A. M. A. **68**:817 (March 17) 1917.

23. Netter: Bull. Acad. de méd., Paris **71**:525, 1914.

24. Schwarz, H.: Poliomyelitis, Arch. Pediat. **33**:859 (Nov.) 1916.

or 67.9 per cent), as shown in table 11, received part of the serum by the intraspinal route, but none of these was treated by the intraspinal method alone. Of the patients who received intraspinal in combination with intravenous or intramuscular therapy, 70.7 per cent recovered without any paralysis. One hundred and fifty-three patients were treated intramuscularly or intravenously alone or by a combination of the two methods. Of these patients, 65.3 per cent recovered without any paralysis, and although this was a smaller group, it was large enough for comparison with the patients given intraspinal therapy. A slightly higher percentage of patients treated by the intraspinal route presented a severe degree of paralysis. Only 10, or 3.1 per cent of the patients treated intraspinally died, as compared to 8, or 5.2 per cent of those who did not receive serum intraspinally. The difference between the two groups

TABLE 11.—*Comparison of Intraspinal and Other Methods of Administration of Serum*

	No. of Patients	Degree of Paralysis										Died		Per Cent of Total Patients Treated
		0		±		+		++		+++				
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	
Total treated intraspinally and intramuscularly or intravenously	324	229	70.7	18	5.5	29	9.0	22	6.8	16	4.9	10	3.1	67.9
Total treated intramuscularly or intravenously	153	100	65.3	18	11.8	15	9.8	9	5.9	3	2.0	8	5.2	32.1
Total number of patients	477	329	69.0	36	7.5	44	9.2	31	6.5	19	4.0	18	3.8	100.0

is not great, but it demonstrates that the patients who received serum intraspinally did not fare worse than those who were not given serum into the spinal canal. In fact, the group who received serum intramuscularly did not fare quite as well as the other groups. The differences throughout are not large, and one may safely say that no advantage was demonstrated for one method of treatment as compared with the others. No harm was done to patients treated intraspinally with human serum in the preparalytic stage of the disease. In most of them the injection of human serum caused a rise in temperature and an increased rigidity of the neck. The spinal fluid usually showed the typical cellular reaction to the injection of serum, namely, turbidity and an increased cell count. These changes were, however, neither as frequent nor as intense as those produced by the injection of horse serum. None of the 10 deaths which occurred in the group treated intraspinally could be attributed to intrathecal serum therapy, since the deaths occurred as the result of bulbar involvement.

COMPARISON OF TREATED AND CONTROL GROUPS

Thus far the various factors which may have influenced the incidence and outcome of the disease have been considered irrespective of whether or not the patients received treatment. Before one can proceed to a comparison of the two groups, however, it remains to determine whether they were comparable and, if not, in which respects they fell short of comparability. In the first place, there were 477 patients in the treated group and only 102 in the control group. There was a difference of over a year in the average age of the untreated or control group as compared with the treated group, the controls being younger. Whereas there were no patients over 14 years of age in the untreated group, 6.4 per cent of the treated patients were in the higher age group. Aycock [25] has shown that the prognosis for older patients is not as favorable as for younger ones. Our comparisons, however, were not greatly disturbed by the difference in age, since only a single death occurred in the older age group. On the other hand, more patients in the control group than in the treated group had low temperatures at the time treatment was begun, one indication that the controls as a whole were less ill than the patients who were treated. As many as 80.4 per cent of the patients in the control group had temperatures of 102 F. or under, and none had temperatures of 104 F. or more (table 3), while only 69.9 per cent of the treated patients had temperatures of 102 F. or under and 1.7 per cent had temperatures of over 104 F. (table 2). Another variant lay in the fact that the control patients were seen on an average somewhat later in the course of the disease than the treated patients. Since in none of them had paralysis developed, one must consider that they were nearer the end of the acute stage of their illness when they first were observed and therefore were less likely to show paralysis.

Ten physicians treated the 579 preparalytic patients included in this report and examined over 200 other patients who were already paralyzed. Since each physician had seen a large number of patients with poliomyelitis previously, he was fairly well qualified to estimate clinically the apparent seriousness of a case when the patient was first seen. Although we realized that a case might not be classified exactly the same by two persons, in order to make comparisons possible we determined to classify all of our patients from the standpoint of the relative seriousness of the condition at the time of the physician's initial visit. The patients were graded according to the following ranks, to which the numerical valuations of 1, 2, 3 and 4 were given, representing the physician's opinion of the degree of seriousness of the condition:

25. Aycock, W. L.: The Significance of the Age Distribution of Poliomyelitis: Evidence of Transmission Through Contact, Am. J. Hyg. **8**:35 (Jan.) 1928.

(1) mildly ill; (2) fairly ill; (3) seriously ill, and (4) extremely ill or not likely to survive. These gradations were made on the basis of the temperature, pulse, respiration, expression, mental state, age and stage of the disease when the patient was first examined. Table 12 shows the patients of the treated group thus classified. We calculated a contingency table showing the final outcome for the treated patients on the basis of this classification. The coefficient of mean square contingency,[26] a statistical measure which is used to express the degree of relationship of various factors between which a correlation may exist, was calculated on the basis of these data. In this case it was +0.61. The highest possible contingency in a threefold classification would be 0.816. Therefore, the contingency + 0.61 may be interpreted as indicating that there was a fairly high correlation between the physician's estimate of the seriousness of the condition at the time of

TABLE 12.—*Comparison of Physician's Estimate and Actual Outcome for the Treated Patients*

Actual Outcome	Physician's Classification				
	Mildly Ill	Fairly Ill	Seriously Ill	Likely to Die	Total
0	108	187	33	1	329
±	15	14	7	0	36
+	8	32	4	0	44
++	6	13	12	0	31
+++	0	12	7	0	19
Died	2	4	9	3	18
Total	139	262	72	4	477
Per cent	29.1	55.0	15.1	0.8	100.0

treatment and the final outcome. The data were analyzed in the same way for the control group. The coefficient here was + 0.58, slightly lower than that for the treated group, but indicating more than a median positive relationship between the physician's estimate of the seriousness of the condition and the final outcome. Comparison of the proportions of the treated and of the control groups placed in these various categories, namely, mildly ill, fairly ill, seriously ill and likely to die, further suggests that the condition of the untreated or control patients was somewhat milder than that of those who received treatment. The condition of 29.1 per cent of the treated patients and of 40.2 per cent of the controls was considered mild in the physician's classification. On the other hand, 15.1 per cent of the treated patients were classified as very seriously ill, as compared to 11.7 per cent of the controls. The number of those considered likely to die was so small that neither group is favored.

26. Yule, G. U.: An Introduction to the Theory of Statistics, London, C. Griffin & Co., 1919, p. 64.

In order to obtain a numerical estimate of the difference between these two groups, it was first necessary to determine the average rank of each group, basing the calculations on the arbitrary valuations 1, 2, 3 and 4. The average rank for the treated group was 1.88, and that for the untreated group was 1.74. Thus, there was a difference of 0.14 in favor of the untreated group, with $\frac{\text{Difference}}{\text{Physician's estimate of difference of the average}} = 2.65$. It is true that 0.14 may seem rather small to indicate any real difference in grade. It must also be borne in mind that the ranks 1, 2, 3 and 4, designating the seriousness of the illness at the onset, are purely arbitrary and only a rough measure at best. These gradations do not lend themselves readily to study by refined statistical methods, but any real difference demonstrated, such as that indicated by the equation just given, would seem significant. Contrary to the experience of Park,[27] who stated that among the hospital patients that he had observed there was no difference in the degree of seriousness of the condition in the treated and the untreated patients, both statistically and by the physicians' personal estimates we found that the untreated patients in our study on the whole presented milder manifestations.[27a]

In addition to the variables already mentioned in the two groups which are being compared, one must consider another, which may be of some importance, namely, the possible variation in the potency of the serum. In collecting serums for use in the present study each donor was examined clinically in order to confirm the diagnosis of poliomyelitis. By far the greatest percentage of persons who presented themselves had crippling evidence of the disease. Some persons who had hemiplegia due to birth injury and other nonpoliomyelitic conditions were readily excluded. There was, however, no simple way of determining which of the chosen donors had potent convalescent serum, since the monkey method for estimating serum potency is expensive and impracticable. Yet there is not a better method available today. Moreover, serum which has been collected in bulk and pooled does not retain a constant virucidal power. Some of the globulin which contains the virucidal substance precipitates out on standing. When this is removed by refiltration, the serum contains less antibody. The loss depends on the bulk of serum that is filtered, a larger quantity losing proportionately less. In spite of the factors mentioned, the pooled serums which were tested throughout the epidemic had about the same potency. Since the serums were used shortly after they were prepared, loss of potency because of precipitation of globulin was not a factor. Another

27. Park, W. H.: Therapeutic Use of Antipoliomyelitis Serum in Preparalytic Cases of Poliomyelitis, J. A. M. A. **99**:1050 (Sept. 24) 1932.

27a. Park's [27] article utilized some of the data which are given in full in this report.

point is the question of the addition of an antiseptic. MacNamara [28] felt that the addition of cresol, U.S.P., or a similar antiseptic destroyed some of the potency of the serum on standing. At the present time, merthiolate is being tested as an antiseptic in place of cresol.

Keeping in mind the variables for the treated and control groups and also the possible variation in the serum potency, one may now compare the outcome in the two groups. As previously stated, the interpretation of the results of the analysis which has been made must take into consideration the fact that symbols have been arbitrarily chosen to chart the end-results in each case. Since, however, we have used the same designation throughout, we feel that the analysis, because of the large number of cases involved, is for our purposes a practical one.

Eighteen of the 477 treated patients, or 3.8 per cent, and 2 of the 102 control patients, or 1.9 per cent, died. The mortality in both the treated and the control group is considerably less than the mortality from poliomyelitis as recorded by the New York City Health Department from July 1 to Nov. 1, 1931, the same period covered by this study. There were during that time in all 4,046 patients, of whom 474 died, a mortality of 11.4 per cent.[29] Our 579 cases, which had a mortality of 3.4 per cent, are included among those on which the calculation of the general city mortality was based; so, excluding these, there were 3,465 other cases of poliomyelitis, with 454 deaths, a mortality of 13.1 per cent. The patients whom we saw in the preparalytic stage of the disease, therefore, fared much better than the patients whose cases were reported to the health department. The latter were for the most part patients who were paralyzed when they were first seen by a physician. There was a greater tendency for the patients who were paralyzed early in the disease to show fatal bulbar paralysis later than for those whom we saw in the meningitic stage. The 1916 epidemic of 8,881 cases in New York City showed a mortality of 27.3 per cent.[16] The diagnosis of preparalytic poliomyelitis was not made as frequently in that epidemic as in 1931, and one may very properly surmise that there were preparalytic cases in that epidemic which were unreported. These certainly would have increased the morbidity and lowered the mortality, for, as has just been shown, the preparalytic cases offer a favorable prognosis. In fact, one might ask whether a patient who is passing through an obvious meningitic or preparalytic stage does not

28. MacNamara, J.: Serum Therapy in Acute Poliomyelitis, Canad. Pub. Health J. **23**:318 (July) 1932.

29. Personal communcation to the author from the Department of Health, New York City.

have a better prognosis than one who becomes paralyzed early in the disease. Our figures tend to substantiate this point of view.

Table 13 compares the status of the two groups three weeks from the onset with that at the final follow-up examination from five to six months later. Four hundred and forty of the 459 treated patients who survived and 98 of the 100 controls were examined at that time. It will be seen that there was progressive improvement in both groups. Whereas 69 per cent of the treated patients had no paralysis at the end of their acute illness, this number had increased to 78.6 per cent subsequently. An additional 17 patients whose condition was previously classified as +, + + or + + + were entirely well. The ± group showed a slight increase, which can readily be accounted

TABLE 13.—*Condition Three Weeks After Onset and End-Results Six Months Later*

	After Three Weeks				After Six Months			
	Treated Patients		Control Patients		Treated Patients		Control Patients	
Status	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
0	329	69.0	72	70.6	346	78.6	83	84.7
±	36	7.5	12	11.7	40	9.1	8	8.1
+	44	9.2	7	6.9	28	6.4	4	4.1
+ +	31	6.5	5	4.9	17	3.9	3	3.1
+ + +	19	4.0	4	3.9	8	1.8	0	0.0
Died of poliomyelitis	18	3.8	2	2.0	..	...	..	...
Died of other conditions	..	...	..	...	1	0.2	..	...
Total followed	477	100.0	102	100.0	440	100.0	98	100.0
Not followed	..		..		19		2	
Original group (less deaths) for follow-up	459		100		459		100	

for by a transfer of patients from the more severely paralyzed groups. The untreated, or control, patients showed even more marked improvement, the increase being from 70.6 per cent who showed no paralysis after three weeks to 84.7 per cent five or six months later. Each of the other groups likewise showed improvement, and there were no patients in the + + + group at the time of follow-up, the 4 patients originally in this group having improved. The table illustrates the fact that an estimate of any treatment of poliomyelitis, if made shortly following the termination of the acute phase of the illness, is useless, since improvement frequently occurs rapidly during the first few months following the acute stage of the disease. This improvement sometimes takes place because of excellent after-care. Frequently, however, the improvement occurs spontaneously, as may be judged from the many patients who have slight paralysis and remain untreated and in whom the condition clears up entirely in a few months. This is well illustrated in table 13 which shows that the improvement occurs in untreated as well as in treated patients. There is certainly no indication that the

treated patients improved more rapidly than the untreated ones. If there were any evidence that the use of serum arrested paralysis at the time of its administration one might expect that recovery would occur more readily in the treated patients. Park [27] in his discussion of the preliminary report of this study stated that there was no difference in the rate of recovery between the treated and the untreated patients. Amoss,[30] in the same discussion, stated that he had followed cases which occurred in Baltimore three years previously and thought that the serum-treated patients recovered faster than the controls in that epidemic. A careful inspection of table 13, however, reveals that in the present series, if anything, the untreated patients improved somewhat more rapidly and completely than the treated ones. We agree with his impression that patients treated in the preparalytic stage who subsequently become paralyzed recover more quickly than those who are paralyzed very early

TABLE 14.—*Patients Who Were Paralyzed When Discharged Compared as to Status at Time of Follow-Up Six Months Later*

	Treated Group						Untreated Group					
	±	+	++	+++	Total	Per Cent Followed	±	+	++	+++	Total	Per Cent Followed
Total cases	36	44	31	19	130		12	7	5	4	28	
Improved but not entirely well	0	12	2	10	24	20.2	0	3	2	4	9	33.3
Cleared up	20	9	15	2	46	38.6	10	3	2	0	15	55.6
Remained same	13	16	8	6	43	36.1	2	0	1	0	3	11.1
Progressed	2	1	2	0	5	4.3	..	..	..	..	..	....
Died of poliomyelitis	..	..	..	..	..	....	..	..	..	..	..	....
Died (other causes)	0	1	0	0	1	0.8	..	..	..	..	..	....
Not followed	1	5	4	1	11	....	0	1	0	0	1	....
Total followed	36	39	27	18	120	100.0	12	1	5	4	28	100.0

in the disease. Although we did not follow many patients who were paralyzed when we first saw them, it was also our opinion that these patients did not improve as rapidly as the patients in whom paralysis developed after treatment in the preparalytic stage. We believe that the pathologic process in those paralyzed quickly is more irreparable than in those in whom paralysis develops slowly and therefore later in the disease.

The resulting paralysis in the untreated or control group was less than in the treated group. There was a larger percentage in whom paralysis failed to occur as well as a smaller percentage of those who showed the severe grades of paralysis and of those who died among the patients not given serum than among the treated patients. Table 14 shows graphically the improvement in the patients who were paralyzed after three weeks of illness. As previously stated, a larger proportion of the control patients showed improvement, and in a smaller proportion the condition progressed or remained about the same.

30. Amoss, H. L., in discussion on papers on poliomyelitis, J. A. M. A. **99:**

SUMMARY

We have analyzed data collected on two groups of patients gathered for the purpose of determining the value of convalescent serum in the treatment of preparalytic poliomyelitis. We do not consider that the question can be answered definitely because in spite of every effort to obtain comparable data, it was not possible to do so. It has been pointed out that it is particularly difficult in the case of medical material to obtain strictly similar groups. The most important point which our study has emphasized is that 579 patients with poliomyelitis were seen early in the course of the disease, of whom 477 were treated by injection of convalescent serum and 102 were untreated. We showed that the sex, age, stage of the epidemic, day of treatment, dosage and method of administration of serum had no influence on the outcome of the disease so far as can be determined statistically, while, on the other hand, the temperature, cell count and general clinical impression could at times be used as an indication of the degree of severity of the illness.

This was the first epidemic in which an attempt was made fairly to evaluate the serum not only by treating patients in the preparalytic stage but by examining and following a number of control patients. We have demonstrated that the outcome for the treated patients was no better, if as good, as for the untreated ones; while the controls were probably somewhat milder, we feel that no advantage was shown by the other group. For this reason it should be possible in the future to obtain a sufficient number of control cases, for our present study has demonstrated that there is no proof that a physician is depriving his patient of an equal chance for complete recovery by not administering convalescent serum. Lacking a substitute therapeutic procedure, it would seem fair in subsequent epidemics to retest the value of potent serum in the preparalytic or meningitic stage of poliomyelitis, using, if possible, exactly parallel or alternate cases for control. If this is impossible, at least comparisons should be made as to the outcome for treated and untreated patients, using as a basis the day of the disease, the symptoms and other factors such as those discussed in this report.

73 East Ninetieth Street.

CONTOUR OF THE CHEST IN CHILDREN

I. ACCORDING TO AGE

S. A. WEISMAN, M.D.
MINNEAPOLIS

For some years I have been interested in the contour of the chest in health and in pulmonary tuberculosis,[1] my observations having been made almost entirely on adults. My studies led me to draw the following conclusions: 1. The normal chest is flat and wide. 2. The tuberculous chest is long, narrow, deep, undeveloped, rounded and primitive in type.

These conclusions aroused many questions. Because of the fact that the chest of the new-born is almost round, as was shown by Scammon [2] (fig. 1), and that the normal chest of the adult has an average thoracic index of 67 per cent in the male and about 70 per cent in the female (fig. 2), as shown by my studies, the question arises: At what point in life does this change in contour take place? Is the change gradual from infancy to maturity, or does it take place at definite periods? Is there a difference between the sexes in regard to the development of the chest? Do age, height, vital capacity, race, scholastic standing and economical status affect the development of the chest? If the chest is deep at maturity, why should one not consider that its normal development has been hindered, perhaps in early life, resulting in an undeveloped primitive type, such as was found in the tuberculous group which I studied, and one that is perhaps prone to tuberculosis?

In order to clear up these questions, I examined about nineteen thousand Minneapolis school children ranging in age from 5 to 18 years. This group included children from thirty schools from cross-sections of the city. Previous investigations of this kind have usually been carried out on only a small number of children selected from restricted areas and from only one type of environment. I was careful to make

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From the Department of Medicine, University of Minnesota, and the Glen Lake Sanitorium, Oak Terrace, Minn.

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1. Weisman, S. A.: (*a*) Contour of Normal and Tuberculous Chests, J. A. M. A. **89**:281 (July 23) 1927; (*b*) Further Observations on the Contour of Normal and Tuberculous Chests, Arch. Int. Med. **44**:29 (July) 1929, and (*c*) Observations on the Contour of Normal and Tuberculous Female Chests, Ann. Int. Med. **5**:907 (Jan.) 1932.

2. Scammon, R. E.: Studies on Growth and Structure of Infant Thorax, Radiology **9**:89 (Aug.) 1927.

this study cross-sectional so that any possible difference in thoracic development resulting from different environments would be discovered. In this report I shall consider the thoracic index in relation to age only.

The thoracic index is the ratio of the depth of the chest to the width. I used the same technic in this study as in my previous studies. The children were stripped to the waist, and the diameters of the chest were taken at the nipple line with an ordinary pelvimeter with a scale graduated in centimeters. Measurements within 1 cm. were considered within the limits of experimental error.

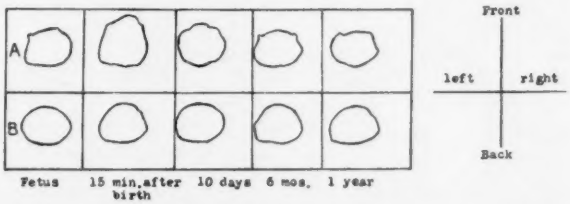

Fig. 1.—Outlines illustrating the change in the shape of the thorax in cross-section at the level of the nipple (*A*) and at the level of the tenth rib (*B*) in the latter part of the fetal period and in the first year. These are based on the data of Calkins and Scammon, Scammon and Rucker, and Richdorf (Scammon, R. E.: Radiology **9**:89, 1927).

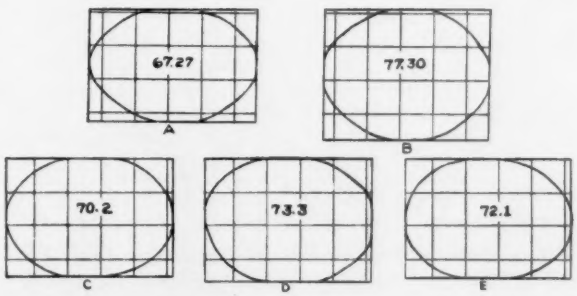

Fig. 2.—Diagrammatic sketches of diameters of chest, with thoracic indexes. (*A*) indicates a normal male chest; (*B*), a tuberculous male chest; (*C*), a normal female chest; (*D*), a tuberculous female chest of the age group of from 16 to 24 years, and (*E*), a tuberculous female chest of the age group of from 25 to 60 years.

THORACIC INDEXES OF SCHOOL CHILDREN

In this series there was a total of 18,557 children. There were 9,438 boys and 9,119 girls, ranging in age from 5 to 18 years. The average thoracic index for the boys ranged from 72 per cent, at the age of 5 years to 69 per cent, at the age of 18, while for the girls it ranged from 71 per cent, at the age of 5, to 70.4 per cent at the age of 18.

It appears that girls have a flatter type of chest before the age of 7. Between the ages of 8 and 10 the boys' chests were definitely flatter than

the girls', but at the period of from 10 years to puberty the girls' chests again took on a flatter contour. It was found that at about the age of 13 the boys again show the flatter type of chest and continue to do so until adulthood.

Brock and Stemmler's [3] study of 522 children of Marburg, Germany, showed that the boys' chests were definitely flatter up to the age of 7 years. From then until maturity the girls showed a flatter type of thoracic contour.

Summary of Thoracic Indexes of 18,557 School Children

Age, Years	Number of Cases		Median		Average		Average Deviation		Standard Deviation		Probable Error	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
5	266	238	727	709	720	710	3.9	3.2	1.54	1.52	±0.063	±0.066
6	784	733	707	719	707	717	3.0	3.57	1.39	1.36	±0.033	±0.034
7	722	826	711	706	718	707	3.47	3.4	1.44	1.41	±0.036	±0.033
8	878	903	703	706	703	707	3.2	3.1	1.32	1.30	±0.032	±0.028
9	986	935	703	703	702	706	3.3	3.2	1.33	1.11	±0.028	±0.024
10	1,015	905	694	692	697	697	3.3	3.6	1.24	1.44	±0.026	±0.032
11	871	843	700	692	700	691	3.7	3.5	1.45	1.42	±0.033	±0.033
12	829	850	699	694	697	695	3.8	3.6	1.59	1.56	±0.037	±0.035
13	733	788	683	690	689	693	3.9	4.2	1.56	1.70	±0.038	±0.040
14	935	854	681	684	682	684	3.9	3.9	1.61	1.68	±0.035	±0.038
15	680	730	681	680	681	682	4.0	4.2	1.60	1.65	±0.036	±0.041
16	500	339	673	681	684	685	4.46	4.3	1.76	1.73	±0.053	±0.090
17	194	141	679	681	678	681	4.4	4.3	1.65	1.50	±0.079	±0.085
18	45	34	679	802	690	704	4.5	4.6	1.88	1.77	±0.189	±0.205

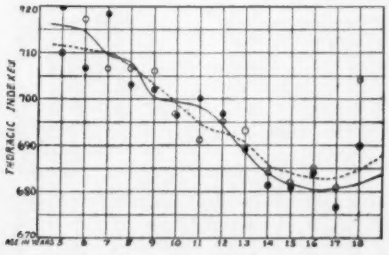

Fig. 3.—Graph showing development of the chest in 18,557 children (9,438 boys and 9,119 girls). In this graph and in figure 4 the circles represent the average thoracic index for each age group. The solid line and black circles indicate boys; the broken line and white circles, girls. The curves were obtained by one application of the three point rule.

Ernst's [4] report on Zurich school children also showed that girls have the better thoracic contour, while Hastings [5] believed that boys

3. Brock and Stemmler: Untersuchungen über den kindlichen Brustkorb, Ztschr. f. Kinderh. **51**:322, 1931.

4. Hoesch-Ernst, Lucy, and Neumann, E.: Das Schulkind in seiner korperlichen und geistigen Entwicklung: Pt. 1. Hoesch-Ernst, L.: Anthropologish-Psychologische Untersuchungen an Züricher Schulkindern nebst einer Zusammenstellung der Resultate der wichtigsten Untersuchungen an Schulkindern in anderen Ländern, Leipzig, O. Menmich, 1910.

5. Hastings, W. W.: Manual for Physical Measurements, New York, The Macmillan Company, 1902.

have a relatively greater width of chest than girls, which corresponds to my findings. These differences, as in the case of the adults previously studied, may be due to geographic distribution, to the technic used and also to the fact that only small, selected groups were studied.

STAGE OF GREATEST CHANGE IN CONTOUR OF THE CHEST

When does the greatest change in the contour of the chest take place between infancy and maturity? Figure 4 presents both Scammon's

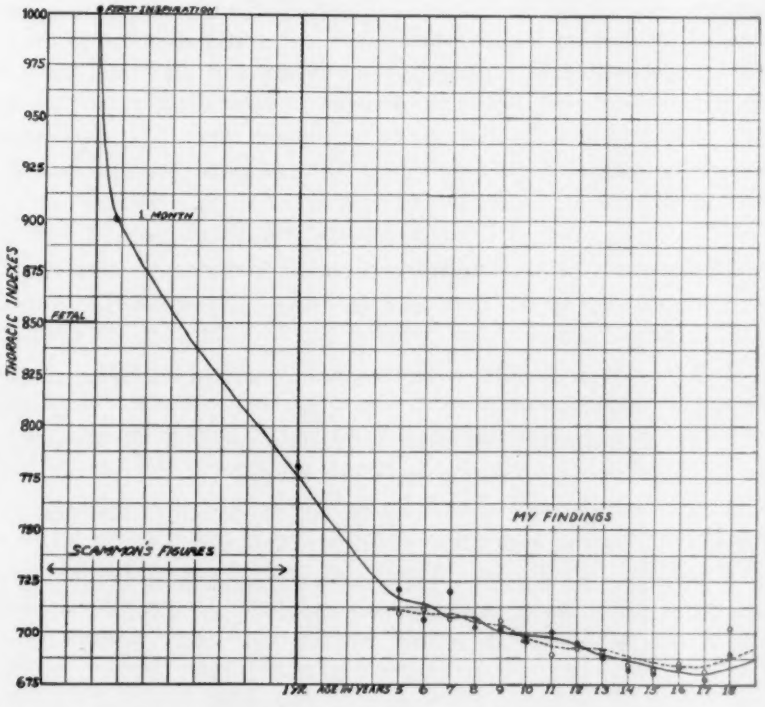

Fig. 4.—Graph showing changes in the thoracic index from the fetal period to the age of 18 years. The lines and circles have the same significance as in figure 3.

findings and my own. It shows the changes in the thoracic index from the fetal state before the first inspiration to the age of 18 years. One immediately observes that at the end of the first year the diameters of the chest have altered considerably. The thoracic index at the end of the first year is 78 per cent. The flattening process must continue at a considerable rate, because at the age of 5 years I found the thoracic index to be about 72 per cent. From then to maturity the change in contour is gradual and slight. My figures tend to show that there is a

difference of about only 5 points in the thoracic index of males between the age of 5 years and maturity, and of about from 2 to 4 per cent in the female chest. In other words, the difference between the thoracic index of the chest on first inspiration and that of a full mature chest is, in all, about 39 degrees. Taking this difference to represent 100, in the first year the chest flattens out about 67 per cent, and by the fifth year it has flattened out about 87 per cent. Between the ages of 5 and 18 years it flattens out only about 13 per cent in males and even less in females. This brings out an important point. It shows that in the first few years of life the contour of the chest changes from the infantile rounded form to the almost mature type. It draws attention to the fact that interest should be centered on the infant and the young child for the greatest and most important study of thoracic development. It is in early childhood that the chest is of the rounded type. May this indicate that the younger the child the greater the danger of tuberculous infection?

CONCLUSIONS

1. The chest of the new-born is almost round.

2. By the end of the first year the chest has flattened to a thoracic index of 78 per cent.

3. As early as the fifth year the chest is almost the same shape as the mature normal chest.

4. The mature form of chest is reached at about the sixteenth to the eighteenth year, when the chest is flattest.

5. About 87 per cent of the changes in the contour of the chest from infancy to maturity take place within the first five years of life.

6. Between the age of 5 years and adulthood there is only 13 per cent difference in the contour of the male chest and a little over 10 per cent in that of the female chest.

FATE OF CHILDREN OF TUBERCULOUS FAMILIES. INCLUDING THOSE TREATED AND THOSE NOT TREATED WITH B C G

C. KERESZTURI, M.D.

WILLIAM H. PARK, M.D.

P. VOGEL, M.D.

AND

M. LEVINE, M.D.

NEW YORK

We started the study of the fate of children in tuberculous homes on Dec. 15, 1926. In 1927, we began to vaccinate some of the children with the attenuated living bovine strain of Calmette, called B C G. In 1931, at the request of Dr. E. R. Baldwin, we added to our procedure the use of heat-killed human tubercle bacilli for an additional small group of children. Up to the present we have administered B C G orally (to new-born children) and subcutaneously or intradermally (to children a few months of age). At first, to study the effects of the vaccine, we vaccinated a few older children by injection. The heat-killed vaccine was given subcutaneously or intramuscularly.

The indications for vaccination were: 1. The child came from a home in which some one had tuberculosis. 2. The tuberculin test, roentgenograms of the chest and physical examination gave negative results before vaccination.

As controls, we tried to select similar children from tuberculous families; these children were later carefully matched with the treated children. Some of them were known to us from birth; others were included in our study within the first or second year of life.

We do not know whether immunity and hypersensitiveness to tuberculin parallel each other. We hope to learn more about this problem in the course of our study. A negative reaction to tuberculin can be converted to a positive one in the majority of cases by vaccination with B C G. Some of the opponents of this form of vaccination claim that a naturally acquired minor tuberculous infection revealed only

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From the Department of Health.

This research was financed by the Metropolitan Life Insurance Company, the Milbank Memorial Fund and the Department of Health. Our co-workers were: M. Sackett, R.N., nurse in charge; G. Richardson, R.N., and S. Stebbins, R.N., assistant nurses; Mrs. Leach, social worker; R. Weber and M. O'Connor, clerks.

by a positive tuberculin test is perferable to vaccination with B C G. This belief does not take into consideration the infected children who die of acute tuberculosis after their primary infection. In order to see clearly in this matter, we are following a special group of patients who gave positive reactions to tuberculin when we first examined them but who showed no other signs of tuberculosis.

Including all of the patients, even those who moved and left no address and those who left the city, we had on Nov. 15, 1932, 435 vaccinated patients and 712 controls. The distribution of these children in the different major and minor groups is seen in table 1.

TABLE 1.—*Status of Groups on Dec. 24, 1932*

Group	Number Receiving BCG Orally; Known from Birth	Number Receiving BCG Subcutaneously; Not All Known from Birth	Number Receiving BCG Intradermally; Not All Known from Birth	Number Receiving Heat-killed Human Tubercle Bacilli	Controls Known from Birth	Controls Not Known from Birth, Entering with Negative Mantoux Reaction	Controls Not Known from Birth, Entering with Positive Mantoux Reaction	Controls Not Known from Birth, Entering Without Mantoux Test
Living subjects being followed	187	33	124	17	193	229	109	14
Subjects who died:								
Deaths due to tuberculosis	2 (0.9%)	...	...	...	6 (2.8%)	8 (3.1%)	9 (7.5%)	
Deaths not due to tuberculosis	27 (12.5%)	...	2 (1.6%)	...	12 (5.7%)	10 (4.0%)	2 (1.7%)	
Composite tuberculous death rate	2 (0.5%)	...	...	...	14 (3.0%)			
Subjects lost sight of	39	...	2	2	26	36	34	24
Totals:								
Minor groups	255	33	128	19	237	283	154	38
Major groups	Vaccinated subjects 435				Controls 712			

The children listed in table 1 were of different ages; some of them were only a few months old at the time of this report, and others were about 6 years old.

None of the children who were vaccinated subcutaneously or intradermally with B C G died of tuberculosis. Two (0.9 per cent) of the children vaccinated orally died of tuberculosis. The controls did not do so well. The lowest mortality due to tuberculosis among the controls (2.8 per cent) was shown by those whom we had known from birth and who were matches for the babies receiving B C G orally. The controls who were in most respects comparable with the patients receiving B C G parenterally, because they gave a negative reaction to tuberculin at the time they entered the group, showed a mortality due to tuberculosis of 3.1 per cent. The patients who had a positive Mantoux

test at the beginning showed the highest mortality due to tuberculosis (7.5 per cent).

If one lumps together all of the children vaccinated with B C G and compares them with the corresponding controls, i. e., those whom we knew from birth and those who gave a negative reaction to tuberculin when we entered them in the study, the difference in the mortality due to tuberculosis is still more striking. It was 0.5 per cent in the composite group receiving B C G and 3 per cent in the composite control group. This means that B C G apparently decreased the mortality due to tuberculosis six times. However, the mortality rate for nontuberculous conditions showed a different trend; it was 1.6 times higher in the group receiving B C G than in the control group. From table 1 it is evident that the patients receiving B C G orally were responsible for the high mortality due to nontuberculous conditions. If one analyzes the 27 deaths among them which were not due to tuberculosis, one finds that about half of the patients died in the first

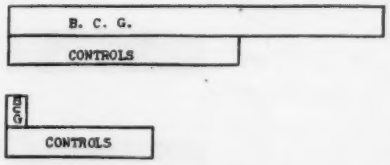

Chart 1.—The upper figure represents the relative death rates from nontuberculous diseases among two groups of children exposed to tuberculosis, namely, 375 who were treated with BCG and 458 who were not treated with BCG. The death rates were 7.7 per cent and 4.7 per cent, respectively. The lower figure represents the relative death rates from tuberculosis among the two groups of children exposed to tuberculosis—0.5 per cent for the group treated with BCG and 3 per cent for the group not treated with BCG. The death rate from nontuberculous conditions among the children treated with BCG was 1.6 times that among the controls. The death rate from tuberculosis among children treated with BCG was six times less than that among the controls.

few weeks of life in hospitals, without going home after birth. They were left in the hospitals because at the beginning of our study we tried to provide for the separation of every baby from the tuberculous focus for one month after vaccination. As we had no other way to arrange this, we put or left the children in hospitals. So many of them died of intercurrent diseases that we thought it wise to give up this practice. After that we did not separate children from their tuberculous parents if we had to hospitalize them.

A summary of the mortality rates of the children receiving B C G and the controls is shown in chart 1.

In order to see whether or not the decrease in the mortality due to tuberculosis among the patients receiving B C G as compared with the mortality among the controls really is significant, one must first decide whether the two groups are comparable. When the mortality due to tuberculosis is in question, the most significant point of comparison is, of course, the presence or absence of exposure to tuberculosis. The children who are exposed to open tuberculosis are most endangered. Children exposed to persons whose sputum is apparently negative are not in such great danger. Finally, there are certain children who, though coming from tuberculous families, are not actually exposed, because the tuberculous member of the family was hospitalized or died

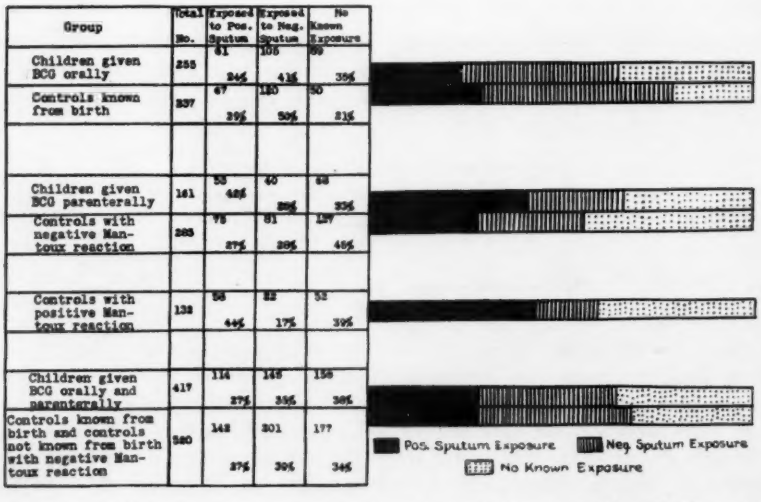

Chart 2.—Difference in exposure between the children receiving BCG and the controls. In the children receiving BCG parenterally and in the controls not known from birth the exposure is considered from the date of vaccination or the date of the first Mantoux test.

before he could come in contact with the child. Chart 2 shows the differences in exposure for the various groups. The exposure was considered from birth for the group receiving B C G orally and for the controls who were known from birth; it was considered from the date of vaccination for the group receiving B C G parenterally and from the date of the first tuberculin test for the controls who were not known from birth (chart 2).

Five per cent less of the children vaccinated orally with B C G were exposed to open tuberculosis and 9 per cent less to closed tuberculosis than of the corresponding controls. In the group parenterally vaccinated with B C G the situation was the reverse; 15 per cent more

of them were exposed to open tuberculosis and 3 per cent less to closed tuberculosis than of the corresponding controls. As the difference in exposure between treated and untreated patients can be considered fairly similar, the sixfold decrease in the mortality rate due to tuberculosis among the combined groups receiving B C G as compared with the corresponding controls is significant.

As an infection with tuberculosis may have an effect as late as three months after the exposure ceases, in the future we plan to tabulate the children parenterally vaccinated with B C G and the controls not known from birth according to exposure, by considering the exposure as dating from three months prior to the vaccination or the first tuberculin test.

The other important point of comparison between the groups receiving B C G and the controls is the age at which the vaccination

TABLE 2.—*The Average Ages of Treated Groups and Controls*

Group	Total Number of Children	Time at Which Age Is Considered	Average Age, Months
Children given BCG orally	255	At time of this report (Dec. 24, 1932)	38
Controls known from birth	237	At time of this report	22
Children given BCG parenterally	173	At time of this report	28
Controls with negative Mantoux reaction	276	At time of this report	37
Controls with positive Mantoux reaction	160	At time of this report	49
Group receiving BCG parenterally	173	At time of vaccination	8
Controls with negative Mantoux reaction	276	At time of first negative reaction	11
Controls with positive Mantoux reaction	160	At time of first positive reaction	17

with B C G was done or, in the unvaccinated group, the time when the subjects entered our follow-up system as controls. Before one evaluates the difference in the mortality rates one must also consider the age at the time of this report. Table 2 shows the average ages in months.

If one tries to interpret the difference in ages from the point of view of the influence on the mortality rate, one might state the following:

1. The controls known from birth were at the time of writing this paper on the average sixteen months younger than the children receiving B C G orally; therefore, the mortality due to tuberculosis would probably increase in the controls until they were as old as the patients who received B C G orally.

2. The group receiving B C G parenterally had to live, on the average, nine months longer in order to reach the age of the controls with the negative Mantoux reaction. Therefore, the death rate due to tuberculosis in these groups would be expected to grow, to the

disadvantage of the patients receiving B C G. If one lumps together the groups mentioned in paragraphs 1 and 2, the age differences probably balance each other in the composite group receiving B C G and the composite control group.

3. The average age of the controls giving a positive Mantoux reaction was 49 months; therefore they had reached an age after which few deaths due to tuberculosis are expected.

4. If one compares the initial ages of the children receiving B C G parenterally, the controls giving a negative Mantoux reaction and those giving a positive Mantoux reaction, one sees that the average ages are 8, 11, and 17 months. This means that the children receiving B C G were the youngest of all of the groups when we accepted them; therefore, on the average, they were followed through a more dangerous period of their lives than were controls giving negative or positive Mantoux reactions. Therefore, it is fair to assume that if the infants in all three groups could have been started at the same age, the difference in mortality due to tuberculosis would have been more to the advantage of the group treated with B C G than we found it.

Summing up our analysis with relation to age, we might say that as a whole the differences in age modify the reality of our mortality rates in tending to give a greater mortality rate to the patients receiving B C G than would have been the finding if all our patients had been entered at the same time and at the same age. When we have sufficient children comprising the different groups, we shall compare the children only when they are of the same age. This analysis with relation to age will then be superfluous, but now it seems important to bring together a grand total in order to have a statistically significant number of cases.

From the point of view of exposure and age we feel that the children receiving B C G and the controls are comparable.

In the future we plan to analyze our observations in relation to the factors of constitution, environment and exposure to tuberculosis, as we have now done with relation to age and type of exposure.

As the detailed analysis of all of our cases is beyond the scope of this paper, we have selected a small but significant group and tried to demonstrate our procedure on it as a sample. The mortality due to tuberculosis and that not due to tuberculosis among 95 children who were known to us from birth and were exposed to open tuberculosis within the first year of life will be analyzed. We limited ourselves to the first year of life because in the later years we had too few cases in each group. The reason for this is partly that all of the children had not finished their second or third year. If we had enough cases in the second year they could be divided into three categories: (1) a group

in which the first year's exposure to open tuberculosis continues, (2) a group in which, in the second year, exposure to negative sputum follows and, finally, (3) a group in which the first year's exposure to open tuberculosis is followed by complete cessation of the contact in the second year. Of course, each of the second year groups has to be similarly divided into three groups in the third year. Therefore, the cases which could be handled in one group in the first year fall into three groups in the second year, and these three groups fall into nine categories in the third year.

Table 3 presents the analysis of the mortality in the first year of life in the treated and control groups known from birth and exposed to open tuberculosis in their first year.

TABLE 3.—*Analysis of Mortality in Children Known from Birth and Exposed to Open Tuberculosis During Their First Year*

Group	Total Number of Children	Deaths Due to Tuberculosis	Deaths Not Due to Tuberculosis
Those receiving BCG orally	54	1 (1.8%)	3 (5.5%)
Controls	41	4 (9.7%)	2 (4.8%)

TABLE 4.—*Frequency of Positive Reactions to Tuberculin* During the First Year*

Group	Total Number of Children	Number Giving Negative Mantoux Reaction	Number Giving Positive Mantoux Reaction	Percentage Giving Positive Mantoux Reaction
Controls	33	23	10	30
Those receiving BCG orally	44	10	34	77

* The dosage for the Mantoux test was 0.2 mg. of old tuberculin.

In the second year there was one more death due to tuberculosis among the controls, but there was none among the children receiving B C G. In the third year there were no deaths due to tuberculosis in either group. As seen in table 3, the similar, heavily exposed, small group treated with B C G showed a mortality rate from tuberculosis that was 5.5 times less than that of the controls. This is very similar to the decrease in our grand totals.

Table 4 gives the comparative frequency of positive reactions to tuberculin in the treated and control groups during the first year of life.

In making up the table we disregarded tuberculin tests made during the first month of life, as not all of the children were tested within the first month, though all those who were tested showed negative reactions at that age. We considered the period between two positive tests positive and that between two negative tests negative; the period between a positive and a negative test, we considered one half positive

and the other half negative. Not all of the children were retested at the end of the year. As seen in the table, in spite of the similar conditions of exposure, the group receiving B C G showed 47 per cent more positive reactions to tuberculin in the first year than did the corresponding controls. Most likely the difference is due to the vaccination with B C G.

ROENTGEN STUDY

Twenty-three of our 41 controls had had roentgenograms made at least once during their lives. Forty-three of the 54 children who received B C G orally had had roentgenograms made. We disregarded x-ray pictures which had been taken and reported on if the films were no longer available for study. Dr. John Caffey, of the Babies Hospital, read the plates for this study.

TABLE 5.—*Roentgen Study (Dec. 23, 1932)*

Group	Total Number of Children	Number Mantoux-Negative and Roentgen-Negative	Number Mantoux-Positive and Roentgen-Negative	Number Mantoux-Negative with Gland Enlargement	Number Mantoux-Positive with Gland Enlargement	Number Mantoux-Negative with Parenchymatous Lesion	Number Mantoux-Positive with Parenchymatous Lesion
Those orally vaccinated who did not die of tuberculosis	42	4 (10%)	20 (62%)	1 (2%)	10 (24%)	...	1 (2%)
Those orally vaccinated who died of tuberculosis	1	...	...	...	...	...	1
Controls who did not die of tuberculosis	18	8 (44%)	3 (17%)	2 (11%)	4 (22%)	...	1 (5%)
Controls who died of tuberculosis	5	...	...	1	...	...	4

As can be seen in table 5, negative films of the chest were less numerous and enlargements of the hilar and paratracheal glands and parenchymatous lesions relatively more numerous among the controls than among the children vaccinated with B C G. It is interesting to note that of the 6 patients who died of tuberculosis only 1 had enlargement of the paratracheal gland alone; the rest of the patients showed parenchymatous pulmonary lesions some time before death. We feel that as far as the roentgen check-up is concerned, the babies vaccinated with B C G made a better showing.

After analyzing the weight curves of the controls and the babies vaccinated with B C G we came to the conclusion that the slightly better nourishment among the latter was explained by the fact that there were fewer premature infants among them. If one disregards the weights during the terminal illness of those children who died there is not

much difference in the nutrition of the children receiving B C G and the controls.

We included in our study two groups of factors which are most likely to influence morbidity and mortality due to tuberculosis. These factors were as follows:

Constitutional and Environmental Factors

1. Weight of the baby at birth
2. Breast and other feeding
3. General condition of the baby
4. Pertussis
5. Measles
6. Other diseases
7. Earning conditions of the family
8. Rooming conditions
9. Ventilation and light
10. Intelligence and cooperation

Tuberculous Factors

1. Length of exposure
2. Intensity of exposure
3. Age of the baby at first exposure
4. Stage of tuberculosis in the source case
5. General condition of the tuberculous member
6. Frequency of positive sputum of the tuberculous member

The 95 aforementioned cases seem to be comparable when analyzed from these sixteen points of view. Therefore, we feel that the difference between the death rates due to tuberculosis among the children receiving B C G and the controls is reliable.

So far as difference in morbidity is concerned, only the roentgenograms give a slight suggestion that the children receiving B C G did better.

SUMMARY AND CONCLUSIONS

Judging from the gross analysis of our total group of over 1,000 children, vaccination with B C G not only is harmless but apparently decreases the mortality due to tuberculosis.

A detailed analysis of observations on 95 children, all of whom were known from birth and all of whom were exposed to open tuberculosis within the first year of life, indicates that the mortality due to tuberculosis was 1.8 per cent in the children receiving B C G and 9.7 per cent in the controls.

The cases were too few to warrant our considering the results more than suggestive that vaccination with B C G prevents a number of children from dying of tuberculosis.

Dr. Rustin McIntosh and Dr. Béla Schick offered suggestions for this work, and Dr. John Caffey read our roentgenograms.

NOTE.—Since this paper was written (Dec. 24, 1932) a newer article on the subject was finished (May 1933) and published (Park, W. H.; Kereszturi, Camille, and Mishulow, Lucy: Effect of Vaccination with BCG on Children from Tuberculous Families, J. A. M. A. **101**:1619 [Nov. 18] 1933).

1225 Park Avenue.

CEREBRAL INJURY IN THE NEW-BORN

ITS RELATION TO CONSTITUTION AND THE TETANY SYNDROME

W. RAY SHANNON, M.D.
ST. PAUL

The confusing frequency of cerebral complications in the new-born, regardless of the type of labor, has resulted in a jumbled mass of uncertain logic revolving perhaps indefinitely but nevertheless accusingly about the pivotal point of obstetric error. That this reasoning has obviously failed to explain the facts has not lessened the burden of responsibility, false though it has often been, foisted on the obstetrician. It is the purpose of this article in a measure to relieve this oppression and to call attention to the frequent existence of a constitutional syndrome during the new-born period which occurs independently of the obstetric procedure and which is often responsible for the symptoms of cerebral disease.

In 1913 Kehrer [1] reported a series of six new-born infants whom he considered as presenting a condition of true tetany. His work was disregarded [2] in spite of the fact that five of these infants responded to calcium therapy in a miraculous manner. In a series of articles published from 1929 to 1931 I [3] reopened the subject, substantiating Kehrer's opinions. Three more contributions, one by Bass and Karelitz,[4] one by McGavran [5] and one by Nesbit [6] have followed, confirming the existence of true tetany in the new-born period and adding a total of ten more cases.[7]

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1. Kehrer, E.: Die Geburtshilflich-gynäkologische Bedeutung der Tetanie, Arch. f. Gynäk. **99**:372, 1913.

2. (*a*) von Reuss, A. R.: Diseases of the New-Born, London, J. Bale Sons & Danielsson, Ltd., 1922, p. 343. (*b*) Grulee, Clifford G., and Bonar, Barnet E., in Haynes, R. S.: Clinical Pediatrics, New York, D. Appleton and Company, 1926, vol. 3, p. 246.

3. Shannon, W. Ray: Generalized Edema in Association with Tetany of the New Born, Arch. Pediat. **46**:549, 1929; A Case of Tetany and Edema in the New Born, Minnesota Med. **13**:476, 1930; Tetany, Generalized Edema and Cerebral Compression in the New Born, Arch. Pediat. **48**:153, 1931.

4. Bass, M. H., and Karelitz, S.: Tetany Accompanied by Hyperpyrexia and Vomiting in the First Days of Life, J. A. M. A. **97**:1372 (Nov. 7) 1931.

5. McGavran, E. G.: Spasmophilic Tetany in the New-Born, J. A. M. A. **99**:115 (July 9) 1932.

6. Nesbit, Harold T.: A Syndrome Occurring in the Neonatal Period Manifesting Tetany-Like Symptoms, Am. J. Dis. Child. **44**:287 (Aug.) 1932.

7. More recently a report by W. M. Taylor has come to my attention. He reported cures by calcium therapy in two cases presenting all three phases of the syndrome. The second of these cases occurred in an infant delivered by cesarean section (Taylor, W. M.: Infantile Tetany, J. Oklahoma M. A. **25**:383 [Sept.] 1932).

It has recently come to my attention, however, that as early as 1910 Sheffield [8] described under the title of "tetanism" a condition which might have some relation to the condition here described. However, the age at which he noticed his syndrome was definitely just after the newborn period, and the condition was accompanied by marked atrophy, a state that was not a necessary part of this syndrome. His later discussion in his textbook does not differ essentially from that early description, and it seems highly improbable that he had in mind the identical condition that I am discussing.

In the evolution of the subject it became apparent to me that the tetany observed in these infants was only a part of a syndrome consisting also of a tendency to generalized edema and edema of the brain and that the last-mentioned symptom was responsible for many of the symptoms usually attributed to cerebral hemorrhage and other injury to the brain. This phase of the subject will be further developed in this article.

From a diagnostic standpoint the most important part of this triad is the tetany. The symptoms consist, in the main, of an extreme nervous irritability, hypertonia, diffuse or localized, often painful spasms of the skeletal muscles, both tonic and clonic, a positive Chvostek sign and exaggerated reflexes. The nervous irritability shows itself in frequent and sometimes almost constant crying with a voice that is often high pitched and piercing and in an increased sensitivity to all sensory impressions such as sudden sound, touch, bright light and slight jarring of the crib.

All the stimuli give rise to much exaggerated responses in the form of sudden movements which vary from a forced stretching action to definite localized or generalized spasms of the skeletal musculature. Such actions usually are apparently painful and they are accompanied by screaming. The hypertonia shows itself as a general tenseness or spasticity of the entire musculature, often with a definite opisthotonos. The most important spasms are those of the hands and feet. The hands may be held in the typical obstetric position, the fists may be tightly clenched or the fingers may be rigidly extended and spread. The feet may be held in a rigid plantar flexion with the toes turned under or extreme extension may be noted. Often one can feel the gastrocnemius muscles, especially, contracted into solid knots. Spasm of the facial muscles may be shown in a constant grimacing or in a pouting position of the lips. Spasm of the extra-ocular muscles may give rise to various movements of the eyeballs, both coordinated and incoordinated. The duration and extent of the spasms vary from slight to most extreme. Usually they are easily precipitated by sudden disturbances of any kind.

8. Sheffield, H. H.: Tetanism, Arch. Pediat. **27**:622, 1910; Tetanism, M. Rec. **81**:846, 1912.; Diseases of Children, St. Louis, C. V. Mosby Company, 1921, p. 671.

While they are typically tonic I observed one case in which striking clonic spasms were present, the groups of muscles varying from time to time. The Chvostek sign has been present in every case in my experience. This reaction has been considered unimportant in the newborn period, but I believe that it has the same significance as at any other age.[9] When one attempts to elicit the Chvostek sign the exaggerated reflexes, aside from the usual responses, give rise strikingly to a sudden closing of the jaw from contraction of the masseters and a quick jerk of the head toward the side from which the impulse comes. Whether these reactions are true reflexes or muscular reactions, they are rather characteristic. The Trousseau phenomenon is difficult to elicit since usually the mere touching of the infant brings about this response. Laryngospasm severe enough to produce cyanotic spells may occur. Electrical reactions have not been obtained.

The subcutaneous edema may vary from a slight puffiness and pitting of certain parts to a tremendously distorting condition causing a lopsided appearance of the entire body from the settling into the dependent parts. It is usually demonstrated earliest in the scrotum in boys, and on the dorsa of the feet and hands in both sexes. A puffiness of the face, especially of the eyelids, is seen early. It is possible for the body as a whole to be dehydrated and yet for these areas of edema to be present. This edematous tendency is shown in an exaggerated swelling over traumatized parts such as the head, the extremities in manipulative deliveries and even areas of hypodermic medication. In extreme cases it seems impossible for injected fluids to be absorbed, the fluid settling inertly into the dependent parts. Occasionally in certain areas, especially in the extremities, the edema may become so severe as to correspond with what has been described as scleredema.

The development of demonstrable edema can usually be presaged in the weight chart. Either the loss of initial weight is slight or absent, or a sudden jump in weight is noted. Once in a while this reaction in weight is noted without definitely demonstrable clinical edema, the so-called preedema of Feer.[10]

The cerebral symptoms are the most important because they are the most grave of all the symptoms of this syndrome. They are the signs of cerebral pressure. The pulse may be slow, though the slowness may not be constant. It may be noticeable only when the infant is perfectly quiet, the normal rapidity returning almost immediately when the infant is made to cry or is otherwise disturbed. In the extreme phase this process may progress into the cyanotic attack. The latter may come

9. (*a*) von Reuss,[2a] p. 73. (*b*) Grulee and Bonar.[2b] (*c*) Mitchell, A. Graeme, and Stevenson, Frank E.: Chvostek's Facialis Sign in New-Born Infants, J. A. M. A. **99**:1502 (Oct. 29) 1932.

10. Feer, Emil: Diagnosis of Children's Diseases, translated by C. A. Scherer, Philadelphia, J. B. Lippincott Company, 1928, p. 58.

on in either of two ways: It may be precipitated suddenly by holding the breath while crying, a mechanism apparently wholly analogous to laryngospasm in infantile tetany, or it may come on gradually while the infant is perfectly quiet. In both cases the heart is slowed almost to a complete cessation of beat, and respiration is suspended for a varying length of time, the infant being to all appearances dead, as indeed he may be. When recovery occurs, its advent may be heralded by a deep gasping inspiration following which both respiration and pulse gradually assume their normal character, or the heart beat may first become somewhat more rapid and stronger, this being followed shortly by the faintest respiratory effort, which, together with the heart beat, gradually assumes its normal character. Usually the cyanosis, which is most extreme in the attack, entirely disappears in the intervals, though this is by no means always true. Respiration is often shallow and irregular. Periods of apnea may be noted, not sufficiently long for cyanosis to develop. It will be noted that this is characteristic of the respiration in alkalosis. At times, when marked tetany is present, one gets the impression that respiratory irregularity may occur as a result of spasm of the diaphragm, similarly to what is noted in other types of tetany. Typical generalized convulsions may occur. Occasionally in severe tetany all the muscular movements of a generalized convulsion, without unconsciousness, may be noted, the infant screaming constantly from the painful spasms which seem to involve most of the skeletal muscles. Projectile vomiting may be a feature. Often a marked mental depression from which the infant cannot be aroused to nurse is noted. On several occasions I have seen infants with this condition who, when fully aroused, showed all of the hyperirritability of the tetanic state until they were permitted to drop back into their state of lethargy. Strabismus, pupillary irregularity and spasmodic downward turning of the eyes may also be noted. In cases presenting these symptoms the diagnosis of increased intracranial pressure may be supported by a definitely bulging fontanel. More frequently the fontanel is merely extremely tense, the sutures being separated and the whole cranium giving the impression of an inflated ball. Additional symptoms suggestive of irregular functioning of the involuntary nervous system may be noted in excessive perspiration, cold and cyanotic hands and feet and delayed or infrequent urination. The last-mentioned symptom may simply signify a lessened urinary secretion, especially in infants in whom edema is developing or marked. One may assume that vomiting and irregularity of intestinal motility may occur on a similar basis, though I have never seen a child in whom this phase was sufficiently striking to be convincing during the new-born period.

All these groups of symptoms, especially the first and the last, are extremely familiar to every pediatrician. The edema is probably much

less so since mild degrees may easily be entirely overlooked and the moderate and severe grades are usually overshadowed by accompanying nervous symptoms. However, the fact that these are in any way related phenomena is not familiar and demands immediate recognition because of the rapidly favorable change that can be brought about by the simple expedient of active calcium therapy.

In table 1 a series of twenty-one cases is presented briefly. Of this number the first eight have been reported previously in detail; the others are new. The diagnoses were made on the basis of the symptoms described.

SUMMARY OF THE CASES

Sex.—In the series there were eighteen boys and three girls. It is interesting to note that infantile tetany is more common among boys.

Labor.—In eleven cases labor was normal. This includes the most severe cases of the series, a fact that speaks strongly against the primary importance of an abnormal delivery as a cause of the symptoms. In this connection I have been permitted to mention a case seen by Dr. L. F. Richdorff in which the entire syndrome, including cyanotic spells, occurred on the second day after a cesarean section and in which the usual response to calcium therapy was obtained.

Age at Onset of Symptoms.—The age at which symptoms are noticed varies from immediately after birth to the seventh day. In the 6 and 7 day group, consisting of four cases, it is not reasonable to believe that the primary cause could have been an injury to the brain at birth in view of the absence of the evidence of such an injury in the interval.

Tetany.—This condition was present in all the cases. It was classed as severe in ten instances, moderate in eight and mild in three. It formed the basis for identification of the syndrome. It yielded to adequate active therapy, not only once but repeatedly. For instance in the twenty-one cases there were at least fifty instances in which there was a disappearance of, or unmistakable improvement in, the condition following therapeutic measures.

Edema.—This was present in all but one case, and in this a marked increase in weight, the so-called preedema of Feer, occurred at the time of the active symptoms. Often the onset of tetany was just preceded or accompanied by a marked increase in weight, indicating that the tetany and the edema were coincidental in development. In every instance therapy directed at the tetany resulted in dramatic improvement of the edema. This occurred not only once but repeatedly. In a total of twenty cases in which edema was demonstrated it showed an unmistakable response to therapeutic measures in at least thirty-eight instances. The edema is naturally more sluggish than the tetany because

TABLE 1.—*Cases in Which Treatment Was Successful*

Case	Sex	Labor	Age at Onset	Tetany	Edema	Cerebral Edema	Duration of Symptoms After Treatment			Number of Therapeutic Responses Till Cure			Treatment
							Tetany	Edema	Cerebral Edema	Tetany	Edema	Cerebral Edema	
1	M. F	Hard, instruments	Few hours	Severe	Severe	Mild ?	3 days	3 days	.....	2	1	..	Calcium chloride
2	M	Normal	6 days	Severe	Severe	Severe	6 days	5 days	Hours	2	2	1	Calcium chloride, parathyroid extract-Collip
3	M	Normal	6 days	Severe	Severe	Mild ?	23 days	24 days	.....	7	4	..	Calcium chloride, calcium gluconate, viosterol, parathyroid extract-Collip
4	M	Normal	4 days	Severe	.....	Severe	5 days	.....	Hours	2	..	1	Calcium chloride, parathyroid extract-Collip
5	M	Normal	7 days	Severe	Moderate	Severe	2 days	2½ days	Hours	1	1	1	Calcium chloride, parathyroid extract-Collip
6	M	Precipitate	Birth	Severe	Mild	Severe	6 days	2 days	18 hours	2	1	1	Calcium chloride, parathyroid extract-Collip, viosterol
7	M	Dry	8 hours	Moderate	Moderate	Moderate	4 days	4 days	Hours	3	2	1	Calcium gluconate, parathyroid extract-Collip, viosterol
8	M	Normal	8 hours	Severe	Severe	Severe	12 days	11 days	3 hours	3	3	1	Calcium gluconate, calcium chloride, parathyroid extract-Collip, viosterol
9	M	Version	18 hours	Severe	Moderate	Severe	2½ days	3½ days	Hours	2	1	1	Calcium gluconate, parathyroid extract-Collip, viosterol
10	M	Hard, instruments	3 days	Mild	Moderate	Severe	4 days	4 days	Hours	2	2	1	Calcium gluconate, parathyroid extract-Collip, viosterol
11	M	Normal	6 days	Mild	Moderate	Moderate	½ day	1½ days	1½ days	1	1	1	Calcium gluconate, parathyroid extract-Collip, viosterol
12	M	Normal	6 hours	Moderate	Moderate	Moderate	11 days	3 days	Hours	1	1	1	Calcium gluconate, parathyroid extract-Collip, viosterol
13	M	Normal	1 day	Moderate	Moderate	Mild ?	6 days	6 days	.....	2	2	..	Calcium gluconate, parathyroid extract-Collip, viosterol
14	M	Normal	6 hours	Moderate	Severe	Severe	4½ days	5 days	Hours	1	1	1	Calcium gluconate, parathyroid extract-Collip, viosterol
15	M	Hard, instruments	10 hours	Moderate	Severe	Severe	6 days	6 days	Hours	3	3	1	Calcium gluconate, parathyroid extract-Collip, viosterol, carbon dioxide and oxygen
16	M	Hard, instruments	7 hours	Severe	Severe	Moderate	5½ days	5½ days	1½ days	3	2	1	Calcium gluconate, parathyroid extract-Collip, viosterol
17	M	Version	6 hours	Severe	Mild	Severe	3 days	2½ days	2 days	3	2	2	Calcium gluconate, parathyroid extract-Collip, viosterol
18	F	Version	6 hours	Mild	Mild	Mild	11 days	2½ days	?	2	1	?	Calcium gluconate, parathyroid extract-Collip, viosterol
19	F	Instruments	3 days	Moderate	Severe	Mild ?	9 days	11 days	Hours	2	2	1	Calcium chloride, calcium gluconate, parathyroid extract-Collip, viosterol
20	M	Normal	3 days	Moderate	Severe	Mild ?	14 days	10 days	Hours	4	4	1	Calcium gluconate, parathyroid extract-Collip, viosterol
21*	M	Normal	4 days	Moderate	Severe	Severe	8 days	8 days	Hours	2	2	1	Calcium gluconate, parathyroid extract-Collip, viosterol, carbon dioxide and oxygen

* I was permitted to participate in this case through the permission of Dr. Woodard Colby.

it is apparent that the fluid does not begin to move until the blood calcium has been altered.

Cerebral Edema.—Evidences of cerebral involvement were frequent. Definite convulsions occurred only in case 2. Convulsions did not recur after therapy was started. Cyanotic spells occurred in seven instances (cases 4, 5, 8, 9, 15, 17 and 21). In not one of these cases did these attacks recur after sufficient therapy had been given to affect the tetany and edema. Three other patients (cases 10, 12 and 14) exhibited periods of marked bradycardia, a symptom which I regard as closely related to the cyanotic spell. In all three the response to therapy was almost immediate. Additional symptoms such as a weak "cephalic" cry, irregularity of respiration, projectile vomiting, tension on the fontanel,

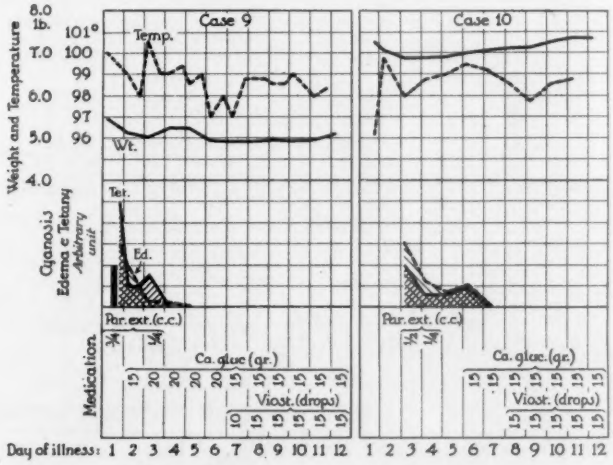

Fig. 1.—Data on cases 9 and 10.

opisthotonos, lethargy and increased pressure of the spinal fluid—symptoms usually given significance in the diagnosis of intracranial involvement—bring the total to 16 or 75 per cent. If one can include such symptoms as a weak cry which cleared up before the therapy was started (cases 1 and 13) and strabismus of a spasmodic character (cases 3, 19 and 20) among the evidences of cerebral involvement, one can raise this total to 100 per cent. In all these cases the response to calcium therapy was dramatic.

Duration of the Symptoms after Therapy Was Started.—In table 1 one finds that in some instances many days were required to control the tetany and edema completely. These prolonged periods were marked by a varying number of distinct therapeutic responses following which, owing either to the transitory effects of parathyroid extract or to too early an interruption in the administration of calcium, the symptoms

* I was permitted to participate in this case through the permission of Dr. Woodruff Coley.

reappeared. In case 3 this process continued over a period of more than three weeks owing, I believe, to a low grade peritonitis from which the infant eventually died. On the other hand, the response of the cerebral symptoms seems to have been much more prompt and permanent, total disappearance usually having occurred within a period considerably

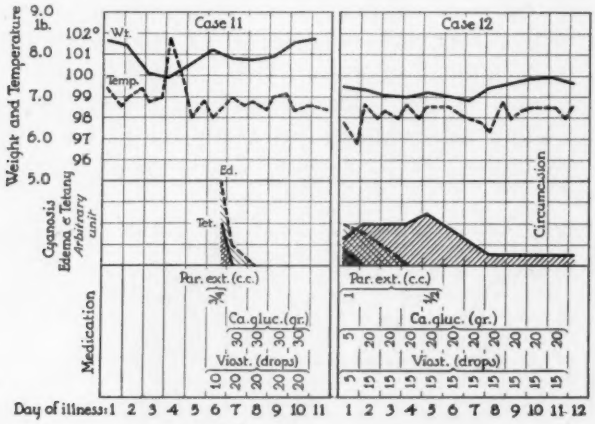

Fig. 2.—Data on cases 11 and 12.

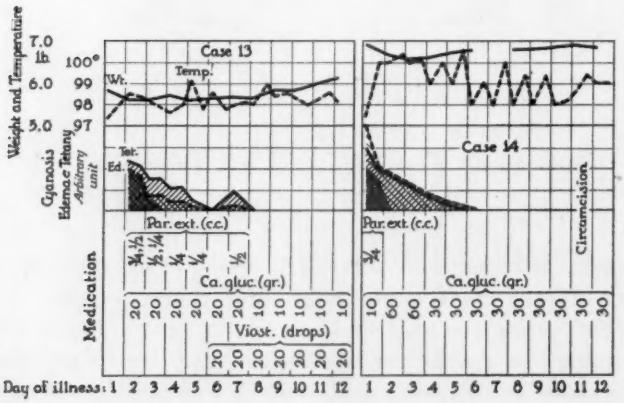

Fig. 3.—Data on cases 13 and 14.

shorter than twenty-four hours. In only three instances did cerebral symptoms reappear after the beginning of the therapy. In case 17 a slow pulse appeared along with a recurrence of the tetany and edema on the third day, only to disappear permanently on further administration of parathyroid extract. In case 18, the twin of this patient (case 17) an increased tension on the fontanel and a spasmodic downward turning of the eyes were noticed for the first time on the eighth day

accompanying a mild tetany while the patient was receiving calcium. In case 21 cyanotic spells recurred on the sixteenth day. These occurred while the patient was on therapy that was inadequate, as shown by a determination for calcium, during an exacerbation of the symptoms of tetany and edema which resulted, I believe, from the subcutaneous injection of a hypertonic solution of dextrose in physiologic solution of sodium chloride. These spells ceased immediately on the intramuscular injection of calcium gluconate, and both tetany and edema had subsided a few hours later.

Treatment.—Treatment consisted of the administration of some form of calcium, the injection of parathyroid extract, and the administration of viosterol. These measures will be completely discussed later. In several cases 5 per cent carbon dioxide in oxygen was administered as an additional measure. The results obtained were no different from those in cases in which this measure was not employed.

COMMENT

Several points not included in table 1 merit discussion at this time. The nature of the cerebral involvement was, of course, not provable. Presumably it was an edema in most instances. There is no way of ascertaining that it was not a hemorrhage. Spinal puncture was not frequently resorted to; it was performed on only four patients of the series (cases 1, 4, 6 and 21). Only in case 1 was macroscopic blood obtained and this was at least in part contamination. Furthermore, the cerebral symptoms were not important in this case. Clear spinal fluid was obtained in each of the other instances.

The subsequent history may be of value in this connection. Of the twenty-one patients one (case 3) died of peritonitis at the age of 5 weeks. Another (case 21) died at the age of a few months of bronchopneumonia following whooping cough. While no postmortem examination was performed, it was thought that the symptoms of cerebrospastic disease had developed before this time. I have followed thirteen of the remaining nineteen patients for periods varying from several months to five years, and none of these have shown evidence of cerebral injury. The remaining six have been heard from, and none show such evidence.

For the establishment of the principle it makes little difference whether hemorrhage was present or not. It is possible that it was present in some, though none of the patients showed localizing signs. Regardless of whether it was present or not, it is evident that therapy was beneficial to the cerebral condition, since improvement was so rapid. The condition which yielded to calcium therapy, it is contended, was an edema of the brain whether or not this edema was accompanied by

any other type of injury to the brain. In the one case (case 21) in which subsequent evidence of cerebral injury sustained at birth seemed to appear there is nothing which makes it certain that the primary injury was in truth a hemorrhage and not a long continued edema and ischemia. There was certainly nothing in the early history to convince one that a cerebral hemorrhage existed.

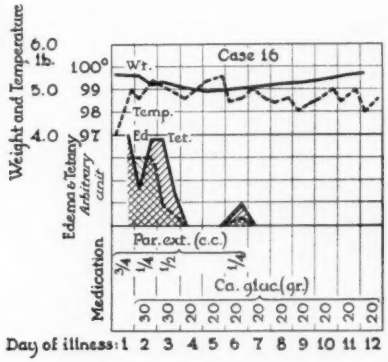

Fig. 4.—Data on case 16.

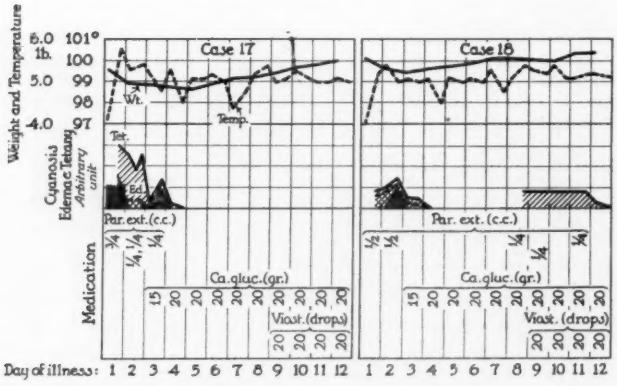

Fig. 5.—Data on cases 17 and 18.

Several symptoms of minor importance have occurred throughout the series frequently enough to require mention. Jaundice is an important member of this group. I am sure that it is not an essential part of the picture, though it is common. It seems more reasonable to believe that it may be a result of an injury to the hepatic cells from a cause identical with that which brings about the disturbed cerebral function. Constant cyanosis was also noted in several cases and occupies an indeterminate position. On the other hand, cold cyanosis of the

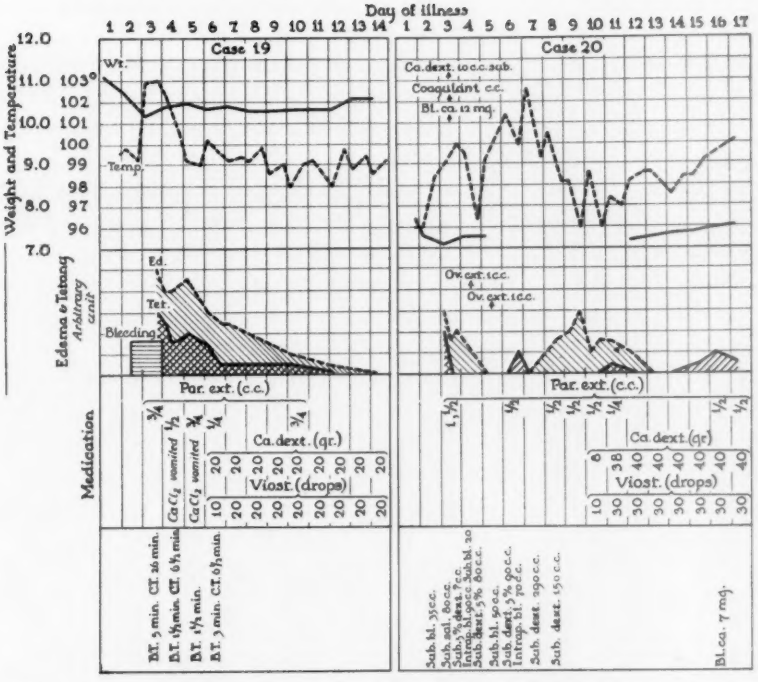

Fig. 6.—Data on cases 19 and 20. B.T., indicates bleeding time; C.T., coagulation time.

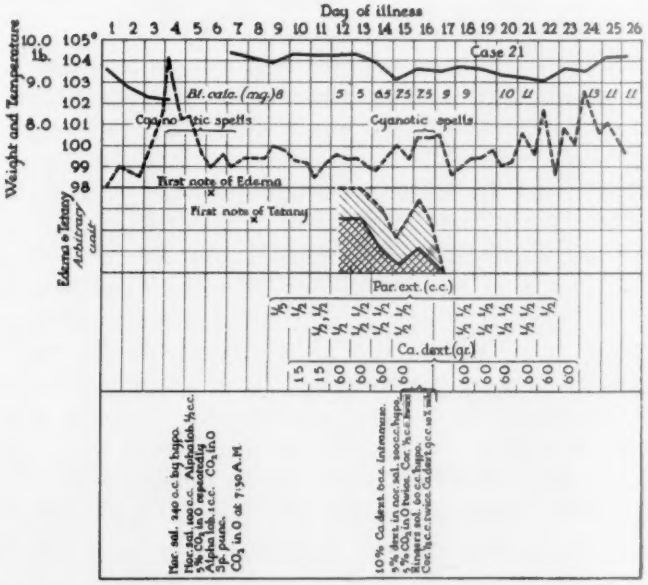
Day of illness
Case 21
Weight and Temperature
lb.
Bl. calc. (mg.)
Cyanotic spells
First note of Edema
First note of Tetany
Edema e Tetany
Arbitrary unit
Par. ext. (c.c.)
Ca. dext. (gr.)
Par. sol. 240 c.c. by hypo.
Par. sol. 120 c.c. Alphalob ½ c.c.
2% CO2 in O repeatedly
Alpha lob. 1 c.c. CO2 in O
Sp. punc.
CO2 in O at 7:30 A.M.
10% Ca. dext. 60 c.c. intraven.
2% dext. in nor. sal. 200 c.c. hypo.
2% CO2 in O twice. Cor. ½ c.c. hypo.
Par. sol. 240 c.c. hypo.
Cor. ½ c.c. twice. Ca. dext. 190 c.c. at 1 A.M.

Fig. 7.—Data on case 21. Alpha lobeline and coramin (cor.) have not been admitted to "New and Nonofficial Remedies."

hands and feet is to be regarded as an integral part of the syndrome, apparently a result of a vasomotor disturbance attributed by Falta [11] to angiospasm. Urinary retention and profuse sweating, when they occurred, were assumed to indicate further disturbances of the autonomic nervous system. Cases 19 and 20 exhibited marked hemorrhagic tendencies. This is not thought to have had a causal relationship with the syndrome.

Values for blood calcium were obtained in only three cases. In case 3 these figures were never very low but were persistently under 10 mg. until the symptoms were permanently under control. In case 20 the first value of 12 mg. was obtained at the time of the first visit. After long continued treatment a value of 7 mg. was obtained at a time when symptoms of tetany, which had been absent, were reappearing. The early high calcium level might be interpreted to mean that at this time a large part of the calcium was inert and was later eliminated. In

TABLE 2.—*Cases in Which Treatment Was Not Successful*

Case	Sex	Labor	Age at Onset	Duration of Improvement	Age at Death	Cause
A	M	Difficult, forceps	Few hours	3 days	5 days	Cerebral edema, hydronephrosis
B	M	48 hours, breech presentation	8 hours	None	14 hours	Cerebral edema
C	M	8 hours, normal	12 hours	5 days	10 days	Sepsis, porencephaly
D	F	Cesarean section	2 days	18 hours	5 days	Influenzal meningitis
E	M	Normal	7 hours	8 hours	24 hours	Cerebral hemorrhage
F	M	.....	Birth	3 days	1 week	Bronchopneumonia

case 21 the low values were very persistent and indicated why so much difficulty was encountered in bringing the clinical symptoms under control. In case 3 the parathyroid glands were histologically normal.

Since failure is perhaps a more accurate test of a theory than success, table 2, comprising cases in which the treatment was not successful, is included.

Case A was encountered early in my experience with the syndrome. In the light of case 21 it is obvious that the therapy was not sufficiently vigorously employed. In case B the infant was practically dead when seen and did not live long enough for the therapy to take effect (death occurred one hour after the administration of parathyroid extract-Collip). The remaining four patients died of causes obviously beyond the help of any therapy. The surprising element in the consideration of these cases is that each showed the syndrome under discussion and that there was a temporary improvement of the symptoms under the therapy. If this apparent coincidence can be logically correlated with the syn-

11. Falta, W.: Ductless Glandular Diseases, Philadelphia, P. Blakiston's Son & Co., 1915, p. 174.

drome, the failures become strong supportive evidence for the theories. This correlation is easily accomplished, as will be seen in the subsequent part.

An analysis of the etiology of this syndrome immediately brings to light its constitutional nature. Since tetany is the universal symptom, it must form the keystone of this analysis. The constancy with which the other symptoms follow its lead in response to therapy make it safe to regard them as due to an identical cause. Figure 8 shows clearly the entire sequence as I believe it to be.

Section *A* represents the clinical syndrome under discussion. Section *B* denotes the specific etiology of *A*. Section *C* in turn tabulates the cause of *B*, while *D* is made up of the factors that produce the condition listed in section *C*. In section *E* are listed the factors that may be

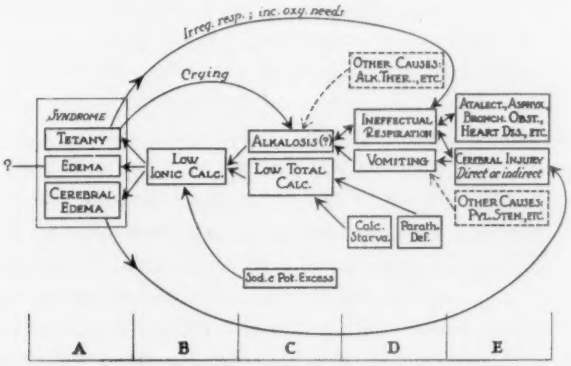

Fig. 8.—Interrelationship of causes and effects in the production of the tetany syndrome.

responsible for the items noted in *D*. All the factors are connected in their proper sequence by arrows. This forms a sequence which expresses with intimate accuracy the steps which eventually may lead to the clinical syndrome that we observed.

Tetany (*A*) is generally recognized as depending on an insufficient content of ionized calcium of the blood and tissues.[12] The latter state (*B*), on the other hand, may occur as a result of several factors (*C*). In the first place it may result from an excess of sodium or potassium.[13] The possible extreme importance of this factor is conceded but so far not demonstrable. Low ionized calcium may also result from low total calcium. Probably the most important contributing

12. Cantarow, A.: Calcium Metabolism and Calcium Therapy, Philadelphia, Lea & Febiger, 1931, p. 139.

13. Marriott, W. McKim: Recent Advances in Chemistry in Relation to Medical Practice, St. Louis, C. V. Mosby Company, 1928, p. 76.

cause, however, is alkalosis.[14] In fact, alkalosis is the only well known mechanism by which a binding of calcium ions is produced, and I believe that it constitutes the most important element in the development of the syndrome described.

There is sound clinical support for this theory. Marriott[15] noted as the clinical signs of alkalosis not only tetany but also shallow, irregular and inefficient respiration, interrupted by apneic pauses of varying duration but sometimes sufficiently long to produce cyanosis. This is precisely the type of breathing frequently noted in cases under consideration. In fact, the breathing of the supposedly normal new-born infant approaches this type.

The theoretical support for the existence of alkalosis is even more convincing (*D*). In general there are three methods by which alkalosis is produced: (1) by the intake of too large an amount of alkali, (2) by too large a loss of acid and (3) by an insufficient production of carbonic acid in the body. The first method is not often of significance in the new-born period and need only be mentioned here. The other two may be very important. Two mechanisms may bring about an excessive loss of acid: vomiting and a disturbance of respiratory origin. Persistent vomiting is generally recognized as a cause of alkalosis and tetany, so-called gastric tetany. It is possible that the three cases reported by Bass and Karelitz and my fourth case were of this type.

To understand the possible rôle of respiration in the loss of acid from the body it is necessary to have in mind something of the function of this mechanism in controlling the p_H of the blood. Since p_H is the principal element in the control of respiration the least change in it is registered in a variation in the respiratory function.

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14. Harrop, G. A. Jr.: Production of Tetany by Intravenous Infusion of Sodium Bicarbonate, Bull. Johns Hopkins Hosp. **30**:62, 1919. Henderson, P. S.: Tetany and the Administration of Alkalies, Quart. J. Med. **13**:427, 1920. Healey, W. P.: Post-Operative Tetany Due to Sodium Bicarbonate, Am. J. Obst. & Gynec. **2**:164, 1921. Denis, W.; von Meysenbug, L., and Goddard, J.: Alkalosis Versus Abnormal Sodium Ion Concentration as a Cause of Tetany, J. Biol. Chem. **57**:47, 1923. Moffitt, H. C.: Tetany in Adults, J. A. M. A. **57**:452 (Aug. 5) 1911. O'Day, J. C.: Gastric Tetany, Northwest Med. **3**:168 (June) 1911. Bircher, E.: Gastric Tetany, Med. Klin. **7**:1223 (Aug. 6) 1911. McCann, W. S.: A Note on Use of Ammonium Chloride in Gastric Tetany, Proc. Soc. Exper. Biol. & Med. **19**:393, 1921-1922. Youmans, J. B., and Green, I. W.: Gastric Tetany, J. A. M. A. **84**:808 (March 14) 1925. Grant, S. B., and Goldman, A.: A Study of Forced Respiration; Experimental Production of Tetany, Am. J. Physiol. **52**: 209, 1908. Goldman, A.: Clinical Tetany by Forced Respiration, J. A. M. A. **78**:1193 (April 22) 1922. Porges, A., and Adlersburg, D.: Tetanie, Wien. klin. Wchnschr. **35**:235, 1922. Porges, A., and Adlersburg, D.: Klin. Wchnschr. **1**:1200, 1922.

15. Marriott, W. McKim,[13] p. 64.

Under ordinary conditions the constancy of p_H is maintained by the interchange between carbonic acid (dissolved carbon dioxide) and bicarbonate. It is expressed by the equation $\frac{H_2CO_3}{BHCO_3}=\frac{1}{20}$. There is a constant relationship between these two which constitutes the first line of defense against a radical change in p_H. Any increase in carbon dioxide constitutes a shift toward the acid side, as a result of which the respiratory rate is accelerated and the excess of carbon dioxide is removed. Any decrease in carbon dioxide is a change toward the alkaline side (alkalosis) and in such a case the respiratory center receives less stimulus, respiration becomes less effective and carbon dioxide accumulates up to the optimum amount. Sustained enforced respiration washes out too much carbon dioxide and leaves an excess of the bicarbonate. The resulting alkalosis may result in the development of tetany.

Coryllos [16] has called attention to the work of Henderson and Haggard [17] showing that in conditions in which prolonged accumulation of carbon dioxide occurred, as in defective respiration, the bicarbonate rises to neutralize the carbonic acid and thus maintain a constant p_H. In this state animals are especially sensitive to hyperventilation. The aforementioned authors have regarded this as sufficient to cause death from anoxemia in dogs before respiration was reestablished by the accumulation of carbon dioxide. Coryllos believes that this mechanism is important in the asphyxial conditions of the new-born. There is much to make one think that it may be an important factor in the development of the syndrome under discussion.

The remaining mechanism for the production of alkalosis is that by which an insufficient amount of carbonic acid is produced. This mechanism is also of respiratory origin and occurs as a result of anoxemia. MacLeod [18] and others [19] have shown that the result of anoxemia in the body is alkalosis. This occurs as a result of the fact that anoxemia itself stimulates the respiratory center to the point at which an excess of carbon dioxide, which is already reduced in amount, is removed. Thus the $H_2CO_3/BHCO_3$ ratio is disturbed toward the alkaline side, and a condition comparable to hyperpneic alkalosis occurs. Haldane [19] has called attention to the irregular type of respiration that may occur from this cause, and it is thus possible that the anoxemia may play a rôle in the irregular breathing seen in this syndrome.

16. Coryllos, Pol N.: Atelectasis, Asphyxia and Resuscitation in the New Born, Am. J. Obst. & Gynec. **21**:512, 1931.

17. Henderson, Y., and Haggard, H. W.: J. Biol. Chem. **33**:333, 1918; quoted by Coryllos.[16]

18. MacLeod, J. J. R.: Physiology and Biochemistry in Modern Medicine, ed. 4, St. Louis, C. V. Mosby Company, 1922, p. 380.

19. Haldane, J. S.: Respiration, New Haven, Conn., Yale University Press, 1922, p. 192.

Such a mechanism should occur with great regularity in the new-born. With respiratory function developing as it apparently does, slowly and in apparent proportion to its needs, it appears that anoxemia of some grade is almost obligatory during this period. If this is true, the slowly increasing efficiency of the respiratory mechanism should keep the infant at least on the verge of alkalosis. The least interference with the respiratory function should immediately increase the anoxemia and thus be capable of greatly enhancing the tendency toward alkalosis.

However, the conception of alkalosis in the new-born does not fit in with the published data on the p_H of the blood at this period. This advances the supposition that not only is there no alkalosis but in reality a mild acidosis occurs at this period. This is adjudged from two main factors: (1) that the alkali reserve of the blood is decreased in the new-born period and (2) that the actual p_H of the blood is lowered. According to Eastman [20] there exists at birth a definite acidosis which is markedly increased by the existence of any degree of asphyxia. Since his observations were made on blood from the cord they have no significance as applied to infants beyond that age. Marples and Lippard,[21] on the other hand, in their series of infants up to the age of 9 days found a normal p_H with a lowered alkali reserve, a fact which they interpreted as indicating a compensated acidosis.

However, a lowered alkali reserve is encountered both in anoxemia and in hyperventilation in spite of the fact that there is a tendency for the p_H to increase.[22] A lowered alkaline reserve is not to be taken as an evidence of acidosis in either of these conditions. Furthermore, in hyperpneic tetany symptoms may develop before any change whatever has occurred in the p_H of the blood.[23] In fact, in one experiment Peters, Bulger, Eisenman and Lee [24] demonstrated the development of tetany when an actual decrease in the p_H had occurred. It may be seriously questioned whether the important factor in these conditions is actually the p_H of the blood or whether it is not some other factor concerned in the $H_2CO_3/BHCO_3$ relationship (release of sodium and potassium ions, etc.). It seems more likely that this may be true.

20. Eastman, N. J.: Foetal Blood Studies: III. The Chemical Nature of Asphyxia Neonatorum and Its Bearing on Certain Practical Problems, Bull. Johns Hopkins Hosp. **50**:39 (Jan.) 1932.

21. Marples, Eleanor, and Lippard, V. W.: Acid-Base Balance of New Born Infants: II. Consideration of the Low Alkalosis Reserve of Normal New-Born Infants, Am. J. Dis. Child. **44**:31 (July) 1932.

22. Haldane,[19] p. 93.

23. McCance, R. A.: Spontaneous Overbreathing Tetany, Quart. J. Med. **1**:247 (April) 1932.

24. Peters, J. P.; Bulger, H. A.; Eisenman, Anna J., and Lee, Carter: Total Acid-Base Equilibrium of Plasma in Health and Disease: IV. The Effects of Stasis, Exercise, Hyperpnea, and Anoxemia and the Causes of Tetany, J. Biol. Chem. **67**:183, 1926.

It becomes apparent, then, that two mechanisms may be commonly operative in the new-born period, either of which would be expected to bring about the lowered alkali reserve commonly noted: anoxemia, which logical opinion must concede probably to be commonly present, and hyperventilation, which, if the former is present, must occur with great frequency. Either is capable of producing alkalosis, or perhaps more properly a disturbed $H_2CO_3/BHCO_3$ ratio. Either, then, should be capable of causing tetany.

If this is true, tetany should be common in the new-born period. It is. It is so common that its minor manifestations have been considered as physiologic. The Chvostek sign is considered as of no importance during the new-born period because it is so common.[9] Yet it is amenable to calcium therapy just as it is during the latter part of the first year. Hypertonicity has been considered a normal phenomenon during this period,[25] the limits between normalcy and abnormalcy being not at all defined. This hypertonicity also yields to calcium therapy. Therefore it is contended that the symptoms of tetany are as common during the new-born period as the theories herein presented indicate that they should be. This fact is presented as a further support for these theories.

More important generally than alkalosis in providing a low ionic calcium content of the blood is a low total calcium (fig. 8, section *C*).[26] It must be remembered, however, that low total calcium does not always mean low ionized calcium.[27] In conditions in which the amount of protein in the blood is markedly reduced low values for calcium in the blood serum are encountered but in this case it is the bound calcium that is deficient, and low ionic calcium, as evidenced by the occurrence of tetany, is not a constant finding. While the protein content of the blood in the new-born is somewhat lower than in the adult, it is not sufficiently low for one to attach significance to it from this angle.[21]

In section *D* of figure 8 the principal causes that might be operative in a low total calcium at this period are indicated. The first of these is calcium starvation. It appears self evident that if throughout her pregnancy the mother did not take in a sufficient amount of calcium, the infant might suffer at birth. However, with an intelligent group of mothers, such as that represented in the series of private patients reported on in this paper, one might believe that, were it not for one

25. Grulee and Bonar,[2b] p. 247.

26. Howland, John, and Marriott, W. McKim: Observations upon the Calcium Content in the Blood in Infantile Tetany and upon the Effect of Treatment by Calcium, Quart. J. Med. **11**:289, 1918. Liu, S. H.: Chronic Juvenile Tetany, J. Clin. Investigation **5**:259, 1928. Salvesen, Harold A.: Function of the Parathyroids, J. Biol. Chem. **56**:443, 1923.

27. Peters, J. P., and Eiserson, L.: Influence of Protein and Inorganic Phosphorus on Serum Calcium, J. Biol. Chem. **84**:155, 1929.

fact, this factor could be disregarded. It has been shown that throughout their pregnancies many women exhibit symptoms of calcium deficiency even on the most liberal diets.[28] In the offspring of such women this factor might not be unimportant. Of the relatively small number of women questioned seven of the mothers in my series showed symptoms of the tetanoid syndrome throughout their pregnancies.

The second, and probably the most important, cause of low total calcium is parathyroid insufficiency.[29] This is the only other known cause of low blood calcium that one can regard as being responsible at this age. There are several reasons for attributing considerable importance to this cause. The condition is probably more prevalent than is generally supposed. It is probably an important factor in the breakdown of calcium metabolism in pregnant women.[30] Since it has a marked inheritable tendency, this suggests the existence of parathyroid deficiency in the offspring of mothers of this type. Thus in such cases the factor of parathyroid deficiency is added to that of possible calcium starvation.

The familial tendency of this factor may be utilized to emphasize still further the importance of parathyroid deficiency. Of the entire group ten infants have been followed whose brothers or sisters are also under my care. Of this group of ten, five have brothers or sisters in whom calcium deficiency has been demonstrated.

The personal history has value also in demonstrating the importance of parthyroid deficiency in this syndrome. Of the entire series thirteen patients have been observed through infancy. In five, definite symptoms of spasmophilia developed later in spite of continuous therapy with calcium and vitamin D. Six more presented at some time definite nervous symptoms which, while not definitely identifiable as those of spasmophilia, nevertheless yielded abruptly to the injection of parathyroid extract-Collip.

According to the present state of knowledge hypoparathyroidism sufficiently severe alone to cause tetany should produce a distinctly low blood calcium. In only eight of the recorded cases of this syndrome were determinations for blood calcium made at the time of active symptoms. Of this number only two (cases 20 and 21) showed calcium values sufficiently low to have been the sole cause of the tetany. It appears, therefore, that this factor alone is capable of causing tetany in the new-born. Much more frequently, the factor responsible is probably a combination of hypoparathyroidism and alkalosis.

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28. Hartley, E. C.: Tetanoid Syndrome in Obstetrics, Am. J. Obst. & Gynec. **19**:59, 1930; Tetanoid Syndrome and Its Relation to Menstrual Cramps, ibid. **21**:725, 1931; Tetanoid Syndrome in Pregnancy, Minnesota Med. **13**:190, 1930.

29. McCallum, W. C., and Voegtlin, C.: On the Relation of Tetany to the Parathyroid Gland and to Calcium Metabolism, J. Exper. Med. **11**:118, 1910.

30. Cantarow,[12] p. 141.

Referring again to the diagram (fig. 8), ineffectual respiration (*D*) is primarily dependent on one of two principal factors. The first of these (*E*) may be identified as any condition interfering with the proper aeration of the blood in the lungs. Primarily important among such conditions would be: atelectasis or any other pulmonary condition interfering with alveolar function; bronchial obstruction, whether due to accumulation of mucus, enlarged thymus or other causes, and cardiac insufficiency, whatever its cause. The second contributing cause would be anything interfering with the nervous control of respiration. This would mean primarily injury to the brain. Such an injury might be gross, such as destruction from hemorrhage or other traumatic injury. Probably much more frequently it would be a result of interference with cellular function in the brain accompanying chemical injury as from a primary anoxemia, traumatic edema or narcosis. After all, it is not a hemorrhage on the surface of the brain that kills, but rather the interference with the function of the brain cells that control the vital processes, the heart and the respiration. Probably these cells are not often immediately affected by the primary gross injury. They are usually affected secondarily as a result of edema, pressure, etc.

The last cause of alkalosis, namely, vomiting (*D*), remains to be discussed. Obviously its principal cause is cerebral injury. It must be recognized that other possible causes exist.

In considering the diagram as a whole it becomes evident that a direct relationship can be traced between the syndrome under discussion and any of the so-called primary pathologic states of the new-born, which are commonly reputed to be the causes of death. By these I mean disturbance of pulmonary function, such as atelectasis and bronchial obstruction, and cerebral injury. This is important because the symptoms that have always been attributed to these conditions have been shown, at least in some instances, to be due to the tetany syndrome. A sequence of perfectly logical events leads directly from either atelectasis and similar conditions or cerebral injury to tetany, edema and cerebral edema. The symptoms of the latter group are indistinguishable from those of either of the former conditions. However, the syndrome may develop in the absence either of primary injury to the brain or of pulmonary abnormality. Thus the symptoms that are commonly attributed to atelectasis and to cerebral trauma and that are usually laid at the door of the obstetric procedure may arise from conditions that have nothing whatever to do with that procedure.

More detailed study of the diagram will make apparent certain important facts: 1. If tetany occurs, the irregularities of respiratory action, coupled with the increased consumption of oxygen resulting from muscular spasm, throw greater burden on the respiratory mechanism and increase whatever respiratory inefficiency already exists. 2. The crying that is so prominent a part of his condition has an

undeniable tendency to increase whatever alkalosis is already present.[31] 3. The cerebral edema that may occur constitutes in reality cerebral injury. Thus it may start the entire process. As has been stated, the cerebral edema may occur long after delivery, as late as the seventh day in my series, at a time when primary injury at birth is logically out of the question. 4. Alkalosis stands in a reversible relationship to respiratory inefficiency and the latter in turn to both cerebral injury and atelectasis. Thus it becomes evident that a primary injury to the brain or atelectasis and similar conditions may, through the mechanism described, cause the syndrome under discussion. But it also becomes evident that the syndrome, and any of the factors that may be responsible for its occurrence, may in turn cause either a cerebral injury or atelectasis. One must therefore consider the general subject of cerebral disease, not from the probably comparatively minor standpoint of injury to the brain at birth as a result of poor obstetric technic, but from the much more important standpoint of a constitutional disease with variable causes, most of which can be at least favorably affected by the simple expedient of calcium therapy.

The crucial point on which this theory swings is that of alkalosis (?). The position of this factor has not been verified by actual analysis. Its presence is most strongly indicated by a mass of clinical data and theoretical reasoning. The theory of the presence of alkalosis is so far opposed by certain scientific data the precision of which cannot be questioned, but their interpretation must be considered as impossible in the present state of knowledge. It is my opinion that these data will eventually be correlated with the clinical facts and that a condition of alkalosis or perhaps rather a disturbance in the $H_2CO_3/BHCO_3$ ratio will be found significant essentially in the manner in which it is indicated in this presentation.

TREATMENT

The rationale of treatment becomes evident on glancing at the diagram (fig. 8). It shows clearly that the syndrome must be considered along with the entire series of events leading up to it. Nevertheless it is obvious that the vulnerable point lies in the level of ionic calcium (*B*), and this can be corrected immediately by the simple expedient of active calcium therapy.

Calcium is the specific for this disease complex. It is most effective when injected intravenously. Calcium chloride may be so injected in amounts of 0.5 cc. of a 5 per cent solution per kilogram of body weight, given slowly. However, it is so extremely irritant outside of the blood vessels that it is dangerous to inject it into the longitudinal sinus. If suitable veins in the scalp or the external jugular veins are available, one of these routes may be used. Considerably safer, if

31. Marriott,[18] p. 60.

somewhat less effective, is the injection of a 10 per cent solution of calcium gluconate. Its less irritant quality makes it safer for intrasinusal injection. Except in very urgent cases it is probably better to inject it into the muscle. I have used as much as 10 cc. without bad local effects, and the dose may be repeated as necessary.

Parathyroid extract-Collip is invaluable. While its effects are less prompt than those following the injection of calcium they are sure and sustained, not only in raising the level of blood calcium but also in raising its effectiveness (increased ionization, Liu). It should be used in conjunction with the other forms of calcium therapy. In urgent cases as much as 1 cc. may be injected, and this may be repeated after from four to six hours if no improvement occurs. I have used as much as 1.5 cc. at a single injection. Usually, however, from 0.5 to 0.75 cc. is sufficient for the first and for repeated injections. Parathyroid extract-Collip should be used until the symptoms are controlled. It is safe, provided the injections are separated by intervals of time sufficiently long to judge the effects of the former dose before repeating. Injections at too short intervals may lead to a cumulative effect and thus cause too high a level of blood calcium, a result which so far I have never observed. The symptoms of tetany form a more delicate index by which to judge the effects of and the necessity for parathyroid extract-Collip than does the edema. The ideal control would be by repeated determinations of blood calcium, but this is obviously impossible in many cases, and the clinical symptoms must usually form the basis of this control.

The administration of calcium by mouth should accompany the other methods. While calcium chloride is by far the most effective salt, it is poorly tolerated by infants and nearly always causes vomiting. Therefore it is better to rely on the less effective but better tolerated salts such as calcium gluconate, calcium lactate, dicalcium phosphate or calcium carbonate. I have usually given 10 grains (0.65 Gm.) of calcium gluconate every four hours. Viosterol either alone or with halibut liver oil should also be given, though its immediate value may be questioned.

Further measures directed at the cause of the low ionic calcium must be instituted (fig. 8, section *C*). As a possible precaution against the excess of sodium it appears reasonable not to employ an unbalanced saline solution for hypodermic injection but to use Ringer's solution for this purpose. Continued calcium therapy is the safeguard against a decrease in total calcium whether it has occurred as a result of parathyroid deficiency or of calcium starvation (*D*).

Alkalosis (*C*) offers a definite therapeutic approach. Vomiting (*D*) should be corrected in whatever proves to be the suitable manner in the particular case, and the amount of chloride so lost should be replaced by injection. It is possible that hydrochloric acid either in a

formula or in water may be of value. Alkali therapy (*D*) is not sufficiently used during the new-born period to warrant its being more than mentioned here. Obviously it should be avoided in these cases especially.

Respiratory inefficiency (*D*), on the other hand, is a factor which must be most seriously considered in the treatment. Two effects must be induced in this effort. The anoxemia must be relieved and excessive loss of carbon dioxide must be prevented. Obviously both of these results are best accomplished by the inhalation of mixtures of carbon dioxide and oxygen after the manner of Henderson.[32]

It may be well to consider some of the possible objections to the use of this treatment. Eastman has objected to the use of this method of resuscitation on the basis of his findings of acidosis in the asphyxiated new-born. His observations, however, were made on blood from the cord. They have no authoritative value in the case of infants who have made the least effective respiratory effort. The overwhelming clinical evidence of the value of this procedure effectively overrides his theoretical objections.[33]

There is, however, a possible danger in the too prolonged use of inhalations of carbon dioxide and oxygen. The observations of Henderson and Haggard on dogs that were kept under conditions of increased carbon dioxide tension over long periods suggest a danger in the use of such an atmosphere for the resuscitation of infants. It is possible that a building up of the bicarbonate level may occur with a subsequent aggravated tendency toward the occurrence of alkalosis from the washing out of carbon dioxide on removal to the ordinary atmosphere. This possibility must be kept in mind and seems to indicate a gradual withdrawal from the carbon dioxide and oxygen atmosphere.

Other measures concerned with the earliest possible establishment of efficient respiration should be carried out precisely as modern resuscitation indicates.[34] Spinal puncture may be valuable in relieving intra-

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32. Henderson, Y.: The Prevention and Treatment of Asphyxia in the New Born, J. A. M. A. **90**:583 (Feb. 25) 1928; Incomplete Dilatation of the Lungs as a Factor in Neonatal Mortality, J. A. M. A. **96**:495 (Feb. 14) 1931; The Inhalational Method of Resuscitation from Asphyxia of the New Born, Am. J. Obst. & Gynec. **21**:542, 1931.

33. Bonar, B. E.: Problems of the New Born, J. Pediat. **1**:92, 1932.

34. Cron, R. S.: Resuscitation of Asphyxiated New-Born Infants, Am. J. Dis. Child. **39**:174 (Jan.) 1930. Flagg, P. J.: Treatment of Asphyxia in the New-Born, J. A. M. A. **91**:788 (Sept. 15) 1928; The Treatment of Postnatal Asphyxia, Am. J. Obst. & Gynec. **21**:537, 1931. Dunham, E. C.: Atelectasis in the New-Born, Am. J. Dis. Child **43**:594 (March) 1932. Murphy, D. P.; Bowman, J. E., and Wilson, R. G.: The Drinker Respirator Treatment of the Immediate Asphyxia of the Newborn (Thirty-Five Cases), Am. J. Obst. & Gynec. **21**:528, 1931.

cranial pressure though I believe that it may be dangerous because of the extreme grade of intracranial pressure that may be present from the swelling of the brain tissue.

One should be able to accomplish much by way of prophylaxis. Certain details available in the history should warn the obstetrician of the possibility of the condition occurring and suggest early preventive measures. Because of the familial tendencies in calcium deficiencies any history of such conditions in the parents or older children should indicate the advisability of extra calcium for the mother throughout the pregnancy. Such a history should forewarn one of a predisposition to this syndrome in the new-born. Unusual asphyxiation at birth calls for immediate steps to prevent the lowering of ionized calcium. Such features may justify the beginning of active treatment as indicated at or shortly after birth. They at least call for a careful watch for the earliest symptoms of the syndrome. Some of the most important of these are a failure to lose weight or a sudden gain, in which case edema must be most carefully watched for; persistence of edema of the head or other sites subjected to trauma, irregularities of respiration with periods of apnea, with or without cyanosis; periods of a slow pulse, often of short duration; cold cyanosis of the hands and feet; projectile vomiting; infrequency of urination; beginning irritability on sudden disturbance; tremors; beginning tension on the fontanel, with separation of the sutures; undue sleepiness, with inability to nurse, etc. The development of these symptoms may be the forerunner of serious involvement of the brain and warrants the beginning of careful and effective therapeutic measures. Last, but not least, prophylaxis requires the best obstetric procedure to prevent, so far as possible, both direct (hemorrhage, etc.) and indirect (narcosis, asphyxia, etc.) cerebral injury.

SUMMARY AND CONCLUSIONS

There occurs frequently in the new-born infant a syndrome consisting of tetany, generalized edema and edema of the brain. This syndrome occurs as a result of some interference with the calcium metabolism which results in a lowered ionic calcium content of the blood and tissues. The possible causes of this deficiency in ionic calcium are the same as those that might be responsible at any age, namely, excess of sodium or potassium, calcium starvation, parathyroid deficiency and alkalosis, and they may and probably do work in combination in bringing on the symptoms.

One of the important factors is thought to be parathyroid deficiency resulting in a lowering of the level for total as well as for ionic calcium, though this factor is probably seldom sufficiently active to be the sole cause of the clinical condition.

The most important cause is thought to be alkalosis, or rather a disturbed $H_2CO_3/BHCO_3$ ratio, which may alone, but more frequently in combination with low total calcium, act as the immediate cause of the symptoms. The alkalosis (?) presumably develops in any of the usual ways but is most frequently of respiratory origin, occurring as a result of the combination of anoxemia with hyperventilation.

Anoxemia is a necessary result of ineffectual respiration and is perforce a common condition in the new-born, since respiratory function is known to develop slowly in proportion to its needs. An obligatory by-effect of anoxemia is hyperventilation due to the stimulation of the respiratory center that occurs in oxygen deficiency, and the hyperventilation, in turn, by washing out the already deficient carbon dioxide upsets the $H_2CO_3/BHCO_3$ equilibrium toward the alkaline side.

There should be a tendency for this to occur even in the presence of a normally developing respiratory mechanism, but in cases presenting any abnormal interference with such development this tendency must of necessity be exaggerated. Atelectasis and similar conditions and cerebral injury, whether direct or indirect, are therefore commonly associated with the syndrome under discussion through the mechanism of alkalosis (?), and the symptoms of all are commonly confused. These ideas are expressed graphically in figure 8.

Since the syndrome is constitutional it follows that the symptoms commonly attributed to cerebral injury and to atelectasis may be of constitutional origin. Therefore the problems of cerebral involvement and of atelectasis and related conditions must be viewed from a more comprehensive angle than merely from that of the obstetric procedure, a factor which in the long run is probably less important than the other elements.

Calcium therapy is specific for the syndrome. This is as true for the serious symptoms of cerebral edema as for the less serious ones of tetany and generalized edema. Since the symptoms of cerebral edema from calcium deficiency are indistinguishable from those commonly attributed to cerebral injury from other causes and are often indistinguishable from those usually credited to atelectasis it follows logically that the hypothesis presented offers an extremely valuable additional method of therapeutic approach in such cases.[35]

35. Since this article was written several additional contributions which advance the theories somewhat beyond the stages expressed have been published: Shannon, W. Ray: Etiology of the Tetany Syndrome in the New-Born Infant, Arch. Pediat. **51**:23 (Jan.) 1934; The Constitutional Origin of Cerebral Disease in the Newborn, Am. J. Obst. & Gynec. **27**:830 (June) 1934. Small, A. S.: Tetany in Young Infants, J. Pediat. **2**:681 (June) 1933. Bloxom, A., and Nicholas, K. O.: Tetany Calcipexicus of the New Born Infant: A Preliminary Report, South M. J. **26**:883 (Oct.) 1933. Maslow, H. L.: Tetany in the New-Born, Arch. Pediat. **50**:768 (Nov.) 1933.

GLOSSOPTOSIS DUE TO ATRESIA AND HYPOTROPHY OF THE MANDIBLE

PIERRE ROBIN, M.D.
PARIS, FRANCE

The article by Eley and Farber [1] of Boston published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN in 1930 seems to me a precise demonstration of the conception which I presented for the first time in 1926 on hypotrophy of the mandible and its consequence, congenital or acquired glossoptosis. Dr. Armand-Delille thought this study interesting and useful and suggested my publishing in the same journal a short notice of our combined research in order to record the results of our experience.

For many years I have studied dysmorphosis of the faciocraniovertebral skeleton, in particular that of the mandible. Hypotrophy of this bone is a determining cause of glossoptosis, which through the respiratory insufficiency that it produces leads to a certain physical backwardness which persists throughout infancy, childhood and adult life.

In 1902 I first showed to different societies in Paris an apparatus, the "monobloc," which allows the reestablishment of the normal relation between the two maxillary bones when they have lost their equilibrium. At the same time the two dental arches come together normally, normal mastication becomes possible and the child is again able to breathe through his nose.

The great majority of children with hypoplasia of the mandible breathe through the mouth. At that time, I was interested only in children having both temporary and permanent teeth. So my treatment concerned only children over 6 or 7 years of age. Most of these children had adenoids, but though the adenoids were removed once or several times they continued to breathe through the mouth and the adenoid facies persisted. Such children show, as a rule, a retracted lower jaw, and because of the retraction of the mandible the floor of the mouth and the tongue are pushed back, obstructing the passage of air when the mouth is closed. The difficulty of breathing is increased because the base of the tongue presses on the epiglottis, and the glottis therefore becomes closed.

This explains why a child who has had adenoids removed is still unable to breathe through the nose, since he still suffers from glossoptosis. I demonstrated that if one forces such a child to propel the

1. Eley, R. Cannon, and Farber, Sidney: Hypoplasia of the Mandible (Micrognathy), Am. J. Dis. Child. **39**:1167 (June) 1930.

mandible forward so that the incisors meet as in biting a thread he immediately becomes able to breathe through the nose and seems entirely relieved.

In 1921 and 1923 I published papers on this subject in the *Bulletin de l'Académie de médecine de Paris,* and on Jan. 2, 1923, I first called the mechanical effect "glossoptosis."

For many years I noticed that the organovegetative and psychic disturbances caused by glossoptosis were more serious when the hypoplasia of the mandible was more pronounced and when the disturbances began earlier. This explains why congenital glossoptosis is more dangerous than acquired glossoptosis.

These observations led me, in 1924, to examine babies. I soon noticed that many cases of congenital hypoplasia of the mandible occurred and that the organovegetative and psychic life of the infants was more disturbed when the hypoplasia was more pronounced. I even observed some cases so severe that I wrote, in 1926, that I had never seen babies live for more than sixteen or eighteen months who presented hypoplasia such that the lower maxilla was pushed more than 1 cm. behind the upper. A whole scale of degrees lies between such extreme hypertrophies and the slight ones which require thorough study before a correct diagnosis can be made.

On the basis of the wonderful cures which I had obtained in children and adults suffering from glossoptosis, I then published a series of studies on orthostatic feeding of infants and the glossal reflex in which I described the treatment of mandibular hypotrophy. I could not hope to have infants wear a monobloc, though I am able to use a monobloc for a child aged 20 months.

In the course of my studies on orthostatic feeding (when a bottle is used, the orthostatic feeding must be fractional), I advised that the glossoptotic, vomiting or colicky child be held on his stomach in order to calm him. I also showed the advantage of having the baby begin to eat lying on his stomach when the mother is still in bed following the birth or when the child is too weak to be held erect.

I related in my book, "Glossoptosis, a Serious Danger for Our Children," some observations that I had already presented to different scientific societies, in particular the Société de pédiatrie de Paris and the Société de médecine de Paris. I shall mention here two of the cases of severe congenital hypotrophy in which the lower maxilla was retracted more than 1 cm. behind the upper.

Both of the infants concerned were born at term and weighed more than 3,000 Gm. They appeared healthy but had never been able to suck at the breast or from a bottle and had been fed entirely with a spoon. They belonged to the populace of Paris and were from birth under the care of the most competent pediatricians, but in spite of all

efforts in their behalf they both died of athrepsia before the age of 18 months. This was the natural outcome of the complications of the dangerous congenital glossoptosis. I managed by means of orthostatic feeding to make one of the children (fig. 1), aged 15 months, gain 50 Gm. in weight weekly for a month; but his condition was so poor that he finally died of mild bronchitis. I could not follow the second child, who was 8 months old when I saw him and died shortly afterward.

These two infants were obviously of the same pathologic type as those whose photographs were shown by Eley and Farber. All of the children had congenital glossoptosis, more or less severe. It will be noted that the baby in case 4 of the American authors, whom it was not possible to save, is the one whose condition approached most closely that observed in my two patients. My patients died of glossoptotic

Fig. 1.—Photographs of an infant with glossoptosis treated by orthostatic feeding.

cachexia, and it is probable that the death of Eley and Farber's patient was due to the same cause, aggravated seriously by cleft palate.

I did not have an opportunity of performing an autopsy on my patients, as did Eley and Farber, but undoubtedly, like them, I should not have found any organic cause to explain the athrepsia and death in spite of the best of care.

Like the American authors, who were able to save three of the infants with glossoptosis by the use of a brace, by placing the infants on the stomach and by special feeding, I have been able to bring a great number of such infants to a normal condition by orthostatic feeding followed by the use of a monobloc.

These observations justify the belief that athrepsia and death are caused by respiratory and nutritional insufficiency following congenital glossoptosis due to mandibular hypotrophy. My researches have been

based on many cases of glossoptosis the severity of which corresponded to the different degrees of mandibular hypotrophy, from that sufficiently pronounced to cause death to simple dysmorphosis of the jaws which can be detected only by careful study and causes only mild complications. Mandibular hypotrophy is never idiopathic. As a rule it is caused by congenital syphilis or tuberculosis, by a hereditary dystrophia from alcoholism or by some other infection. Occasionally a mild case occurs in the child of parents one of whom has large jaws and the other narrow ones; the child has a narrow upper jaw and a broad lower one, or vice versa, so that there is a lack of equilibrium between the two, and functional troubles appear.

In a general way, glossoptosis and functional respiratory disturbances are due to the functional disequilibrium previously mentioned, which is also the cause of compression of the nasopharynx, the effects of which are revealed by the physical and psychic manifestations constituting the *"glossoptotic syndrome."*

By taking impressions each month of the jaws of infants with congenital glossoptosis subjected to orthostatic feeding, it is sometimes easy to observe the progressive advance of the mandible at the same time that the glossoptosis is cured and the organovegetative and psychic life becomes normal. The photographs shown in figure 2 illustrate this. One observes, moreover, that after a certain time the nasopharynx which was congested progressively becomes free, making the passage of air constantly easier. Breathing through the mouth is replaced by breathing through the nose, which is the only normal method, as has been shown conclusively by George Rosenthal.

It is important to determine at the birth of the child that he sucks normally. Otherwise, just as a badly milked cow fails to give milk after a few days, the mother's milk will become scanty, the baby will lose weight, and finally the milk will be entirely exhausted and the baby will have to be fed from a bottle.

I have never tried the use of a bandage to help the forward propulsion of the mandible, as have Eley and Farber, because my experience with the use of a bandage for children wearing a monobloc was not a success. Indeed, when I tried to employ a bandage on children between 3 and 12 years old at the beginning of the treatment, to help them to shut the mouth on the monobloc, the parents always complained that the bandage, in spite of special care, slipped backward and squeezed the neck, inducing coughing and even augmenting the breathing by mouth. Therefore, I did not try to use a bandage on infants, fearing that the same difficulties would arise. Probably with a helmet like the one devised by the American physicians, the bandage would hold better than with the three-piece bonnet that I used. Nevertheless, I shall adhere to the method of orthostatic feeding, which gives excellent

results and does not present the inconvenience of a permanent bandage or brace. I should not imply, however, that orthostatic feeding prevents the use of a bandage.

In orthostatic feeding the baby sucks with his thorax held up straight so that he lifts his neck and propels his chin forward, as do cubs, calves, colts, puppys and baby monkeys when they are sucking. In order to feed her child orthostatically the mother is obliged to hold herself erect, with the breast elevated and the thorax held up. This obviates a disadvantage of the usual method of feeding with the baby lying on the knees of the mother, in which the breast, especially if it is voluminous, weighs on the chin of the child, as does also frequently the hand of the mother, tired of holding the nipple. Moreover, all adults know how difficult it is to drink lying down, and why should it not be equally difficult for babies?

I have insisted also on the importance of not having the baby lie down after the meal. On the contrary, he should be held erect and

Fig. 2.—Results obtained on the jaws of an infant with glossoptosis by the use of orthostatic feeding. The model designated *7* shows a retracted lower jaw in an infant 5 weeks old. He sucked badly and lost weight, and the mother's milk became scanty. He was given orthostatic feeding. After three months (model *3*), the lower jaw had advanced, the child had gained in weight and the mother had more milk. After eight months of orthostatic feeding (model *6*), the two maxillae came together exactly, the child was normal in weight, and the mother's milk was abundant.

without being shaken be carried about for ten minutes, until he has expelled the air taken in with the milk and begins to fall asleep.

As a result of this method of feeding I have seen babies that had vomited since birth and had not gained in weight begin to drink regularly, without vomiting, the normal ration of milk for their age and gain steadily in weight.

It is also important to hold a baby with glossoptosis on his stomach as soon as he cries or seems worried, in order to prevent gurgling and other causes of respiratory disturbance. When the glossoptotic baby is on the stomach the tongue naturally falls forward by its own weight; the nasopharynx is then free, and the air easily passes into the pharynx, preventing lateral compression of the vessels of the neck. Moreover, the nasopharynx being free, there is no more stagnation in the pharynx of saliva and septic mucus coming from the cavum, which can be

pushed by gurgling into the eustachian tube and infect the middle ear, causing otitis, or slip into the throat, producing suffocation and cough and even involving the lungs and the respiratory passages.

It is easy to see how the work of Eley and Farber confirms my ideas on this subject. As these physicians stated, babies with congenital glossoptosis due to mandibular hypotrophy are from birth difficult to nourish. These patients, I should add, require throughout life special care to enable them to fight against the disturbances caused by the glossoptosis.

For a great many years I have called the attention of pediatricians and general practitioners to the danger of glossoptotic respiratory insufficiency in children. I have also tried to establish the relation between retardation of physical and psychic development in children and glossoptotic respiratory insufficiency, as these developmental defects exist long before the growth of adenoids and persist long after their removal, until the glossoptosis is cured. These observations lead me to say that *I have never seen adenoids without glossoptosis, but I have at times seen glossoptosis without adenoids.*

Laryngologists consider children who do not improve in general health after the removal of adenoids and who continue to breathe through the mouth as afflicted with "adenoidism," that is, as "adenoid without adenoids." Such adenoidism becomes, therefore, for the laryngologist a morbid entity of unknown cause. However, the diagnosis of glossoptosis is sufficient to clarify the pathologic basis of adenoids, which is merely glossoptosis, curable by relief of the glossoptosis, with or without adenoids. Patients with adenoid glossoptosis are noticeable by their general appearance—breathing with open mouth, retraction of the lower jaw and appearance of fatigue. The pale face, black and blue eyes, pinched nostrils and blank expression leave no doubt of the respiratory insufficiency. The whole organovegetative life of such children is slowed. They are generally backward in every way. As a rule, at school they are absent-minded and unstable and follow the lessons poorly even though they may have vivid intelligence. They are often difficult to manage and quick-tempered. Though their health is much improved during the holidays, when they return to school they lose the rosy cheeks, weight and appetite that they have gained. They are always tired and lean against the wall or furniture, bending forward with stooping shoulders. They have difficulty in running, lose breath easily and are subject to stitches in the left side. They masticate poorly and keep the mouth open, swallowing air and becoming aerophagic and aerocolic. They often have accumulation of gas in the stomach, concomitant gastro-intestinal troubles and infections, generally accompanied by constipation and by appendical or hepatic crises. Suffering from respiratory deficiency, they frequently have colds in the

head, and sore throat, and the colds generally involve the chest. The thorax is poorly developed, the apexes and bases of the lungs being poorly aired, so that they remain congested. These localized stases predispose the children to tuberculosis.

As these patients generally present vagosympathico-endocrine instability, they walk and talk late. They are often considered lazy, when they are in reality merely sick children who will become normal and active after the proper treatment. Indeed, when treated by the eumorphic method, these children frequently become calm and thoughtful, make progress in school and become normal in a short time.

The wearing of the monobloc is never painful, and many children become so accustomed to it that they cannot go without it. By this treatment, the appearance of the patient is improved, and the temporomaxillodental articulation gains perfect equilibrium.

It is understood that the children must be kept under the general care of a physician, on a special diet if necessary, with climatic treatment and heliotherapy. Appropriate medication for the general condition must be applied after the adenoids have been removed and the monobloc adjusted in the mouth.

ACETARSONE IN THE TREATMENT OF OSSEOUS LESIONS OF EARLY CONGENITAL SYPHILIS

CLARENCE F. FRIEDMAN, M.D.
BROOKLYN

Since 1921 there has been much reference in the literature to the treatment of congenital syphilis by the oral administration of arsenic preparations. Fourneau [1] and Levaditi and his colleagues [2] were the first to make practical use of the drug discovered by Ehrlich in 1908, and designated by him 594. This corresponds to preparation 190 of Fourneau. Chemically it is the acetyl derivative of 3-amino-4-oxyphenylarsonic acid. Recently the drug has been officially accepted in the United States under the name of acetarsone.[3] In reviewing the literature one is struck by the unanimity of opinion regarding the efficacy of this preparation when given by mouth in the treatment of infantile syphilis. Oppenheim,[4] Tuscherer,[5] Soldin and Lesser,[6] Dupérié, Cadenaule and Clarac,[7] Bratusch-Marrain,[8] Nedelman,[9] Rosenbaum [10] and

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From the Pediatric Department, Jewish Hospital of Brooklyn.

1. Fourneau, E.: Sur l'emploi de l'acide oxyaminophénylarsinique et des acides arylarsiniques en général dans le traitement des spirilloses et des trypanosomiases, Ann. Inst. Pasteur **35**:571 (Aug.) 1921.

2. Levaditi, C.; Navarro-Martin, L.; Fournier, L.; Guenot, L., and Schwartz, A.: Recherches sur l'action curative et préventive de l'acide acetyloxyaminophenénylarsinique administré par voie digestive dans la syphilis, Ann. Inst. Pasteur **36**:729 (Nov.) 1922.

3. Acetarsone in New and Nonofficial Remedies, Chicago, American Medical Association Press, 1930, p. 73.

4. Oppenheim, M.: Spirocid bei Syphilis, Wien. klin. Wchnschr. **39**:627 (May 27) 1926.

5. Tuscherer, J.: Zur Behandlung der Lues congenita mit Spirocid, Monatschr. f. Kinderh. **45**:62 (Sept.) 1929.

6. Soldin, M., and Lesser, F.: Weitere Erfahrungen mit Spirozid bei Säuglingssyphilis, Deutsche med. Wchnschr. **54**:958 (June 8) 1928.

7. Dupérié, R.; Cadenaule, P., and Clarac, J.: Sur un cas de syphilis héréditaire précose traité par le stovarsol ou 190, Gaz. hebd. d. sc. méd. de Bordeau **45**: 456 (July) 1924.

8. Bratusch-Marrain, A.: Wert und Durchführung der Spirocidbehandlung der Syphilis im Kindesalter, Arch. f. Kinderh. **92**:26 (Nov.) 1930.

9. Nedelman, E.: Erfahrungen mit der Spirozidbehandlung der Lues congenita, Jahrb. f. Kinderh. **134**:89 (Dec.) 1931.

10. Rosenbaum, H. A.: Stovarsol in the Treatment of Syphilis in Infants and Children, Am. J. Dis. Child. **44**:25 (July) 1932.

Maxwell and Glaser [11] are among those who have added indisputable evidence of the value of this drug when properly employed. All are agreed that it causes prompt disappearance of the clinical symptoms and signs of the disease, although slower in its effect than the arsphenamines and bismuth. The eruption has been shown to disappear in four or five days, pseudoparalysis and lesions of the mucous membrane within a week, snuffles in from four to six weeks, complete recession of a large liver and spleen in from three to four months and a reversal of the Wassermann reaction in from three months to one year.

As a further check on the efficacy of this drug I decided to watch its effect on the lesions of bone of infantile syphilis. I have been unable to find in the literature any reports of a systematic and intensive investigation of this nature, although Nedelman [9] mentioned that in infants with Parrot's disease the roentgenograms show progressive healing of the lesions of bone. Also, Abt and Traisman [12] reported the use of this drug in six infants under 1 year of age, all of whom showed osseous lesions before the treatment was started. Roentgenograms taken after a nine week course of treatment showed complete healing of the lesions. Mettel [13] used acetarsone in the treatment of syphilitic periostitis in children and observed healing, but he was dealing with a late or tertiary manifestation as all of his patients ranged from 6 to 12 years of age.

The infants selected for this investigation were all under 1 year of age. All showed unmistakable clinical and serologic signs of syphilis and, in addition, all showed the osseous lesions of infantile syphilis as demonstrated in roentgenograms. Furthermore, none had had the advantage of prepartum antisyphilitic treatment of the mother, and no infant had any form of treatment other than the administration of acetarsone.

REPORT OF CASES

CASE 1.—E. B., a white boy, was admitted to the pediatric clinic of the Jewish Hospital when 2½ months of age. During the previous week he was extremely irritable, was unable to move the right arm and had swellings on the fingers of both hands. Examination revealed a good state of nutrition; pseudoparalysis of the right arm; swelling and induration about the right elbow joint, especially on the medial surface; spindle-shaped enlargement of the proximal phalanges of the left hand and slight enlargement in the right hand; prominent veins in the scalp; the spleen just palpable at the costal margin; the liver palpable one fingerbreadth below the costal margin; a circinate, brownish, maculopapular eruption on the

11. Maxwell, C. H., and Glaser, J.: Treatment of Congenital Syphilis with Acetarsone (Stovarsol) Given by Mouth, Am. J. Dis. Child. **43**:1461 (June) 1932.

12. Abt, A. F., and Traisman, A. S.: Stovarsol in the Peroral Treatment of Congenital Syphilis, J. Pediat. **1**:172 (Aug.) 1932.

13. Mettel, H. B.: The Use of Stovarsol in the Treatment of Syphilitic Periostitis in Children, Arch. Pediat. **48**:761 (Dec.) 1931.

thighs, and a brownish, vesicular and papular eruption on the soles. The Wassermann and Kahn tests of the blood were both 4 plus. The reaction of the mother to these tests was 4 plus. Roentgenograms taken on admission showed typical osseous lesions of syphilis (fig. 1). Acetarsone was prescribed in ascending dosage and, after treatment for four weeks (total dosage, 6.59 Gm.), other roentgenograms

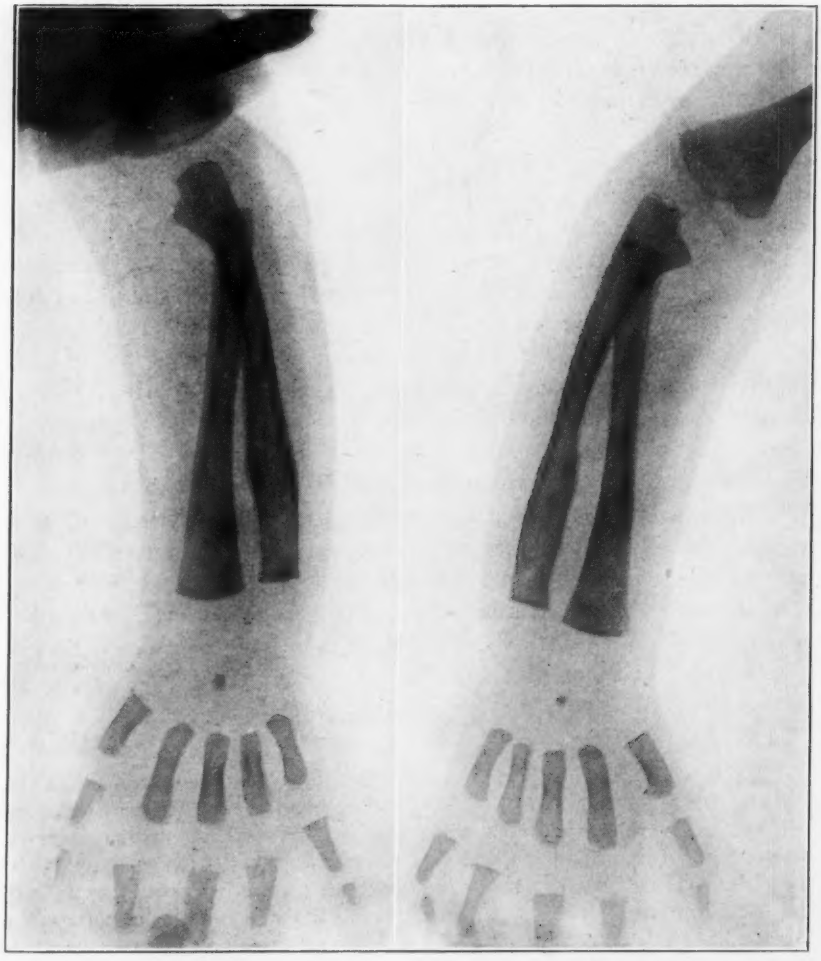

Fig. 1 (case 1).—Bones of the forearm before treatment. There is increased metaphyseal "capping" with patchy areas of submetaphyseal rarefaction (McLean: Am. J. Dis. Child. **41**:363 [Feb.] 1931) at the distal ends of the radii and ulnas. The distal sixth of each radius shows a "punched-out" area of loss of cortex on the lateral surface (osteomyelitis). In addition there is periosteal layering of all the bones of the forearm.

were taken. These showed marked healing of the pathologic process, and only a slight periostitis remained. Figure 2 shows the result of treatment for ten weeks (10.67 Gm.). The effect on the Wassermann and Kahn reactions of the blood

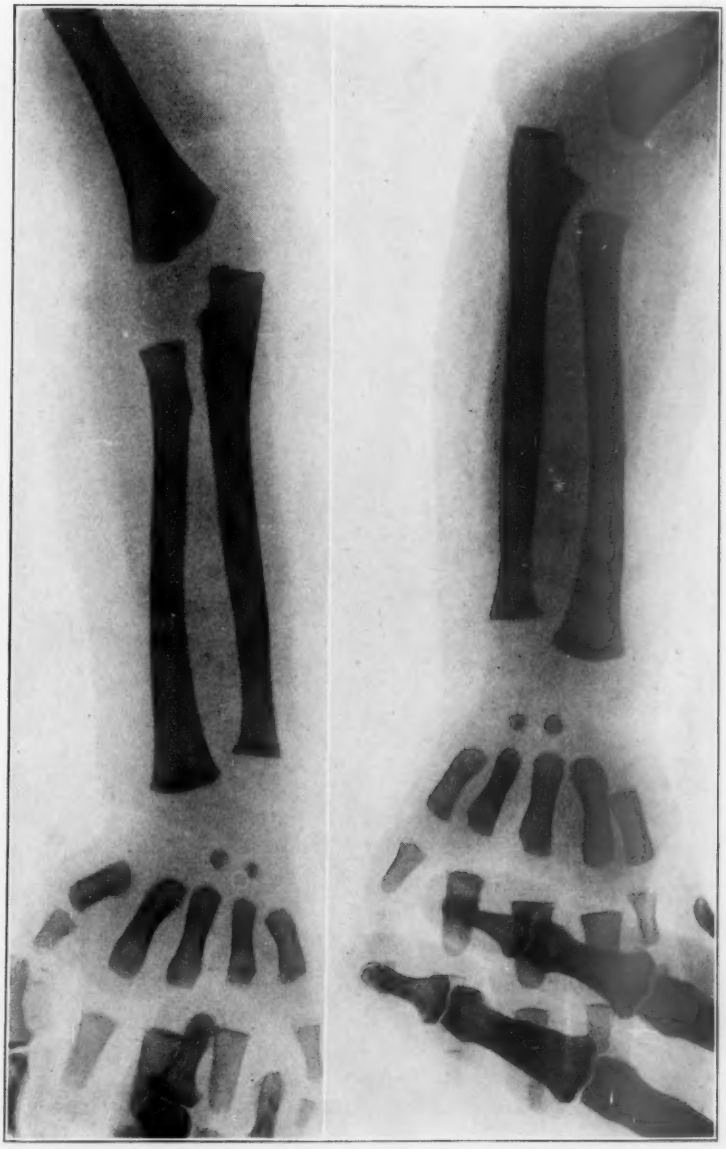

Fig. 2 (case 1).—The appearance of the bones of the forearm after ten weeks of treatment with acetarsone (10.67 Gm.). Note the normal contour of the bones and the almost normal density. Only slight evidence of periosteal elevation persists.

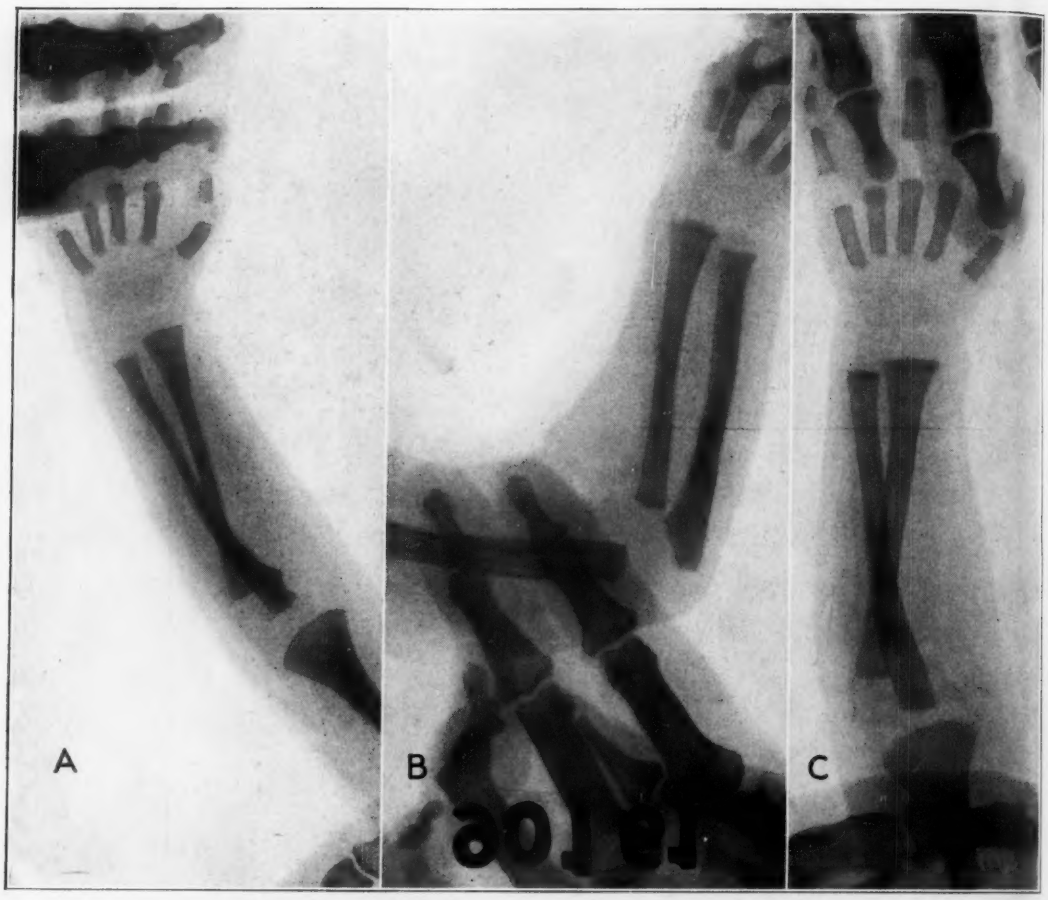

Fig. 3 (case 2).—The right upper extremity: *A*, before treatment. There is marked periosteal stripping of both bones of the forearm, with osteochondritis at the extreme distal end of both bones. There is also ill-defined submetaphyseal rarefaction at both ends of each bone. The distal end of the humerus also shows an area of submetaphyseal rarefaction. *B*, after 1.26 Gm. of acetarsone, given over a period of thirty days. Periosteal layering of the humerus, bones of the forearm and metacarpal bones is marked. This is indicative of healing (McLean: Am. J. Dis. Child. **41**:393 [Feb.] 1931), especially so in the picture presented by the humerus. There are many rarefied areas in the cortex of both the radius and the ulna, but the osteochondritis shown in *A* is not evident. There is a defect in the film about 1 inch from the proximal end of the ulna. *C*, after 5.94 Gm. of acetarsone, given over a period of nine weeks. The bones of the forearm and the lower end of the humerus appear practically normal. There is still slight evidence of periostitis in the metacarpal bones.

was as follows: After four weeks (6.59 Gm.) the Wassermann reaction was 2 plus and the Kahn reaction 4 plus; after four months (15.47 Gm.) the Wassermann and Kahn reactions were negative. After a second and third course of the drug (15.36 and 15.08 Gm., respectively) the Wassermann and Kahn reactions of

Fig. 4 (case 2).—Practically normal upper extremities after 14.94 Gm. of acetarsone had been given.

the blood were still negative, and the Wassermann and Kahn and colloidal gold reactions of the spinal fluid were also negative. At 1 year of age the patient weighed 23 pounds and 2 ounces (10.6 Kg.). He had four teeth at the age of 14 months, and he walked and talked.

Fig. 5 (case 3).—The lower extremities before treatment. The upper and inner sixth of each tibia shows ill-defined osteomyelitis. A similar but more pronounced lesion is found at the lower end of each fibula on the lateral aspect. There is periosteal layering of the tibias and the left fibula.

Fig. 6 (case 3).—The lower extremities after 2.88 Gm. of acetarsone had been given over a period of three weeks. The osteomyelitic lesions described in figure 5 show a definite tendency to heal. The periosteal layering is more marked and is now present on the right fibula as well.

CASE 2.—G. R., a white boy, was admitted to the pediatric clinic at the age of 3 weeks. He weighed 6 pounds and 3 ounces (2,806 Gm.). The infant was one month premature, and weighed 5 pounds and 12 ounces (2,608 Gm.) at birth. The mother's blood showed a 4 plus reaction before the birth of the child, but no prepartum antisyphilitic treatment was given. The reaction of the cord blood

Fig. 7 (case 3).—The lower extremities after 4.44 Gm. of acetarsone had been administered. The symmetrical osteomyelitic lesions shown in figure 5 are no longer visible. There has been subperiosteal formation of new bone resulting in widening of the shafts of the bones of the legs. This is especially noticeable on the medial surface of the right tibia.

was 4 plus, and a roentgenogram of the long bones showed syphilitic osseous lesions (fig. 3 *A*). Physical examination revealed the following: a small, obviously premature infant in poor general condition, with snuffles and bilateral wrist-drop present, the spleen just palpable, the abdomen markedly distended, rapid respira-

tion and crepitant râles in the lower portion of the right axilla. Treatment with acetarsone was begun at once. After 1.26 Gm. had been given the bones of the right forearm appeared as in figure 3 *B*. After treatment for eight weeks (5.10 Gm.) the Wassermann reaction of the blood was "doubtful" and the Kahn reaction 1 plus. One week later, after receiving 5.94 Gm. of the drug, the long bones appeared as in figure 3 *C*. After the first and second course of treatment (14.94 and 25.08 Gm., respectively) the Wassermann and Kahn tests of the blood were nega-

Fig. 8 (case 4).—The lower extremities before treatment, showing the periosteal elevation of the medial surface of the tibias. With a reading glass periosteal elevation of both surfaces of the upper third of the right fibula can be seen. Osteochondritis is present on the lateral tip of the distal end of the right femur.

tive. At the age of 1 year the child weighed 23 pounds (10.4 Kg.). He held the sitting position with difficulty, and had three teeth. The liver and spleen were both palpable one fingerbreadth below the costal margin. There were no other signs of congenital syphilis. The appearance of the long bones after 14.94 Gm. of the drug had been given was as shown in figure 4.

CASE 3.—C. J., a colored boy, was admitted to the pediatric clinic at the age of 2 months, with the chief complaint of difficulty in breathing through the nose. Birth was normal. Both parents were known to have had 4 plus Wassermann reactions of the blood. There was no prepartum antisyphilitic treatment of the mother. The infant was in good condition, and the only positive physical findings

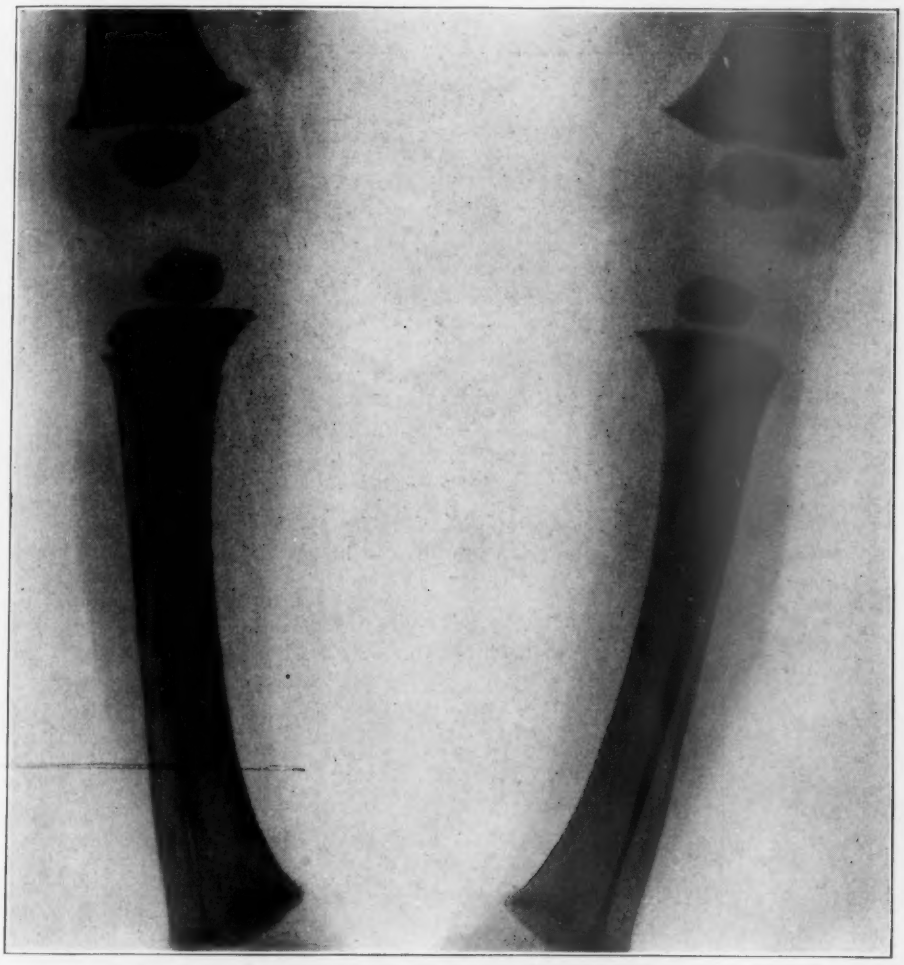

Fig. 9 (case 4).—The lower extremities three months following the ingestion of 3.72 Gm. of acetarsone. The distal ends of the femurs are normal. On the medial surfaces of the tibias can be seen marked healing of the former subperiosteal abnormality.

were: a serosanguineous nasal discharge causing marked obstruction, a spleen that was just palpable and a palpable epitrochlear gland on the right side. Wassermann and Kahn tests of the blood were 4 plus. The roentgenogram of the lower extremities showed syphilitic lesions of the bone (fig. 5). A film of the upper extremities was not made at this time. Acetarsone was prescribed and, after

2.88 Gm. had been given over a period of three weeks, the bones appeared as in figure 6. After 4.44 Gm. of acetarsone had been given a roentgenogram showed marked healing (fig. 7) and the Wassermann and Kahn tests of the blood were both negative. After a course of 15.06 Gm. the Wassermann and Kahn tests were still negative. The patient was readmitted after an absence of five months, at which time the Wassermann and Kahn tests of the blood were negative, and physical examination revealed no evidence of syphilis. He was 15 months of age,

Fig. 10 (case 5).—A roentgenogram of the left upper extremity taken on admission. There is periosteal "cloaking" of the bones of the arm. The proximal and distal ends of the radius and ulna show osteochondritis and submetaphyseal rarefaction. The density of the shafts of the bones of the forearm is not uniform owing to the many areas of rarefaction.

weighed 21 pounds (9.5 Kg.) and was 31 inches (78 cm.) tall. He could speak single words and could stand alone, but could not walk. He had twelve teeth.

CASE 4.—C. W., a colored boy, 3 months of age, was admitted to the pediatric service of the Jewish Hospital on Aug. 21, 1931, with the diagnosis of acute diarrhea with dehydration. The patient was the sixth child. The first two children

died of pneumonia in infancy. The third pregnancy resulted in a premature infant at the sixth month of gestation. The fourth and fifth children were living and well. The birth of this patient was normal, but there was a history of nasal obstruction since birth. Roentgenograms of the upper and lower extremities taken on August 22 revealed changes indicative of syphilitic infection (fig. 8). On

Fig. 11 (case 5).—The lower extremities before treatment. Osteochondritis is present at the proximal ends of the fibulas and tibias. The proximal ends of the fibulas show submetaphyseal rarefaction, and periosteal elevation is present on both tibias, the left fibula and the metatarsals. The network of white lines seen in the upper metaphysis of the right tibia represents a defect in the film.

August 24 Wassermann and Kahn tests of the blood were 4 plus. One week after admission the child had fully recovered from its acute illness. There was no clinical evidence of syphilis except a slight diffuse cloudiness of the corneas and a palpable spleen. Tests of the mother's blood were negative. On September 8

the patient's blood gave Wassermann and Kahn reactions of 4 plus. On September 9 treatment with acetarsone was begun and, after seventeen days of treatment (3.72 Gm.), the parents took the child home against advice. After an interval of three months, during which time it received no antisyphilitic treatment, the child was readmitted to the ward for the treatment of a mucous cyst of the gums. The corneas were now clear, and there was no other clinical evidence of syphilis. A roentgenogram of the lower extremities made at this time is shown in figure 9.

Fig. 12 (case 5).—The left upper extremity after only 0.48 Gm. of acetarsone had been administered. The improvement in the general appearance of the bones of the forearm is striking (compare with fig. 10). The osteochondritis at the ends of the radii and ulnas is definitely healing.

The Wassermann and Kahn tests of the blood were 1 plus. After 9.24 Gm. of acetarsone the Wassermann and Kahn tests of the blood were negative. The patient was discharged to the clinic for further treatment, but he never reappeared.

CASE 5.—D. G., a white girl, was admitted to the pediatric service of the Jewish Hospital on Nov. 23, 1932, at the age of 4 months, with a history of cough and poor appetite of three days' duration. The family history was irrelevant, and

the birth and neonatal histories were normal. The child was acutely ill, presenting the typical clinical picture found with acute pneumonia. Physical examination bore out the clinical impression. Wassermann and Kahn tests of the blood on admission were 4 plus, and these tests on the father and mother were 2 and 4 plus, respectively. A roentgenogram [14] of the left upper extremity taken on the day of admission showed osseous lesions of congenital syphilis (fig. 10). On December 5 a roentgenogram of the lower extremities also showed these lesions (fig. 11). The patient made an uneventful recovery from the pneumonia, and on December 7 the positive physical findings were: baldness, with the exception of a ring of hair

Fig. 13 (case 5).—The lower extremities after treatment with 0.48 Gm. of acetarsone. Osteochondritis is still present at the proximal ends of the fibulas and tibias, but shows a definite tendency to heal (compare with fig. 11). It is highly probable that some of the morphologic changes seen in these bones, especially at their distal ends, are due to concomitant rickets.

14. Some of the lesions shown in the films in this case are undoubtedly rachitic. Therefore, some of the improvement shown in subsequent films is due to the healing of these lesions under the influence of cod liver oil. However, it cannot be expected that cod liver oil therapy would cause the apparent rapid healing of the syphilitic lesions.

in the occipital region; a general glandular enlargement, including the epitrochlears; a high arch of the hard palate, and a liver and spleen palpable two fingerbreadths below the costal margin. The changes in the spinal fluid and the reaction to the colloidal gold test were negative. Administration of acetarsone was begun on December 12, and on December 19, after 0.48 Gm., the bones of the extremities appeared as in figs. 12 and 13. The child was then discharged from the hospital, and was followed in the clinic. Roentgenograms of the long bones were again

Fig. 14 (case 5).—The left forearm after treatment with 3.06 Gm. of acetarsone over a period of eight weeks. The bones are in a stage of advanced healing.

made after 3.06 Gm. of acetarsone had been given over a period of eight weeks (figs. 14 and 15).[14] At this time the Wassermann and Kahn tests of the blood were both 4 plus. The patient was not brought back for further treatment.

The plan of dosage used in treating the infants in this series was, at first, the ascending method recommended by Tuscherer.[5] For the most part, however, the dose was computed according to body weight, from 10 to 20 mg. per kilogram being given daily. This is somewhat

after the method of Bratusch-Marrain.[8] At least three courses, each consisting of from 15 to 20 Gm., were advised. During a course of treatment no rest periods were given except when vomiting, diarrhea or acute illness intervened. No toxic effects of the drug were noted in this series with the exception of case 2, in which a mild attack of vomiting and diarrhea and a morbilliform eruption on the torso developed after 3.42 Gm. of acetarsone had been taken. After a rest period of one week treatment was resumed without untoward effect.

Fig. 15 (case 5).—The lower extremities after treatment with 3.06 Gm. of acetarsone. The osteochondritis shown in figures 11 and 13 has entirely healed. Periosteal elevation is still present on the tibias and right fibula, but there is marked evidence of subperiosteal regeneration of bone.

I believe that the roentgenograms presented give graphic evidence of the healing of the lesions of bone of early congenital syphilis under acetarsone therapy. In some cases these lesions would undoubtedly heal without therapy of any kind, but such healing would probably occur only after a long period. An example of such a case would possibly be the syphilitic infant who recovered spontaneously from the clinical

manifestations of the disease only to become the victim of a recurrence at a later age. In four of the five cases reported here healing of the osseous lesions was demonstrated after short periods of treatment and after small doses of the drug.

SUMMARY

The successful treatment of congenital syphilis with arsenic preparations administered by mouth has been reported by many authors in recent years. The drug most commonly used has been the acetyl derivative of 3-amino-4-oxyphenylarsonic acid, now officially known as acetarsone. There is practically uniform agreement among investigators concerning the efficacy of this preparation in clearing up the clinical signs and symptoms of the disease, and in reversing the positive serologic reactions.

This study was undertaken in order to determine the effect of the oral administration of acetarsone on the osseous lesions of early congenital syphilis. Five cases are presented, all of which showed the clinical, serologic and roentgenographic signs of infantile syphilis. In no case had there been prepartum antisyphilitic treatment of the mother. Acetarsone by mouth was the only form of therapy used. The age of the patients at the beginning of treatment varied from 3 weeks to 4 months. Roentgenograms of the long bones taken before treatment and at varying intervals during treatment are presented. These demonstrate the prompt healing of the syphilitic lesions of bone.

CONCLUSIONS

The oral administration of acetarsone is of value in the treatment of early congenital syphilis. Moreover, it is a relatively safe, easily controlled and an agreeable form of therapy. Additional evidence of its efficacy in bringing about a "cure" is attested by its ability to promote the healing of the osseous lesions of infantile syphilis.

ANATOMY AND PHYSIOLOGY OF THE GALLBLADDER IN CHILDREN

A CHOLECYSTOGRAPHIC STUDY

EDWARD A. BOYDEN, PH.D.
AND
ALICE H. FULLER, M.D.
MINNEAPOLIS

The present study consists primarily of a comparison of the evacuation of the gallbladder in children with the emptying of that viscus in young adults, and is a continuation of a preliminary study made several years ago.[1] It is, therefore, an attempt to add to the meager knowledge of the physiologic changes which accompany the growth and development of the gastro-intestinal tract in human beings.

The methods employed were similar to those by which the norm of the adult organ was established.[2] Each gallbladder was visualized by oral administration of tetra-iodophenolphthalein—from 2 to 3 Gm. in grape juice, given in two successive doses the night before roentgenograms were made. The next morning, after preliminary films were made, roentgenograms were immediately made again, and the patient was given a glass of yolks of three eggs stirred in milk. Roentgenograms were then made two, four, eight, twelve, sixteen, twenty, twenty-five, thirty, thirty-five, forty, fifty and sixty minutes after ingestion of food or as near these intervals as the exigencies of the case permitted. In the interests of economy roentgenograms were not usually made after the first hour, yet this period was ample to cover the principal phase of contraction. Special care was exercised to keep all conditions as uniform as possible.

Forty-one children between the ages of 6 and 11 years were subjected to this technic. All were hospital patients made available through the courtesy of Prof. Irvine McQuarrie, chief of the pediatric service of the University Hospital. As indicated in table 2, all but four were

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From the departments of Anatomy, Pediatrics and Child Welfare, University of Minnesota.

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1. Boyden, E. A., and Birch, C. L.: Emptying of Gall-Bladder in Children, Proc. Soc. Exper. Biol. & Med. **26**:312, 1929.

2. Boyden, E. A.: An Analysis of the Reaction of the Human Gall-Bladder to Food, Anat. Rec. **40**:147, 1928.

convalescing from conditions other than disturbances of the gastro-intestinal tract, so that they were considered virtually normal for the study of the function of the gallbladder.

Owing to the difficulties of making roentgenograms of children of this age—their frequent inability to hold their breath without abdominal twitching and the presence of intestinal gas in such quantities as would suggest pathologic conditions had we been dealing with adults—only twenty-eight of the series of forty-one (twelve girls and sixteen boys) were available for statistical study. After the outlines of 400 of the gall-

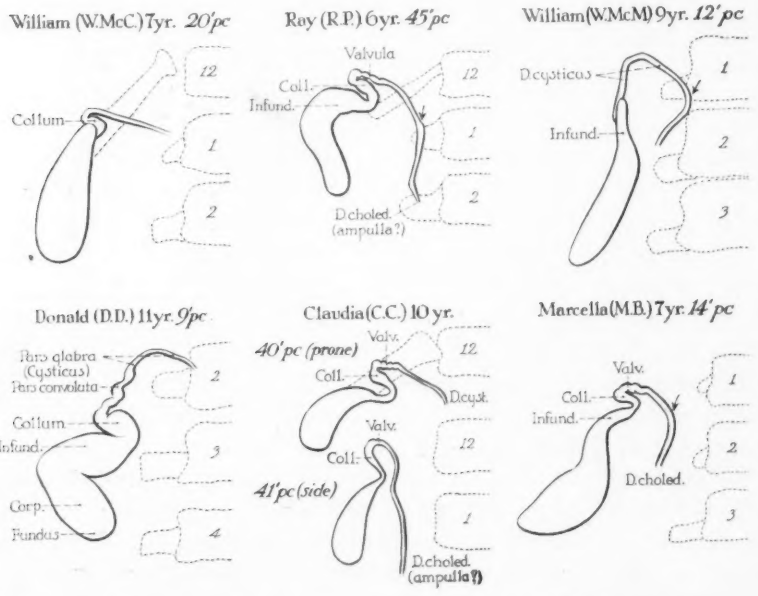

Fig. 1.—Tracings of cholecystograms selected to show the position and parts of the gallbladder in children. Additional pictures of C. C. are shown in figures 2 and 5 and of R. P. in figure 4. A computation of volumes may be found in table 2. The arrow indicates the probable position of the hepatic duct. Gallbladders in which the valves of Heister are not visible (W. McC.) may empty more slowly than those in which the valves are most conspicuous (C. C.; table 2). Reduced from × 215 (two thirds).

bladder shadows had been transferred to tracing paper, the volume of the fundus, body and infundibulum was computed by means of the graphic method described in full in a previous publication.[2]

As the present study has revealed additional details of the position of the gallbladder in the living patient and since this has direct bearing on the computation of volumes, it has seemed preferable to discuss the anatomic relations first.

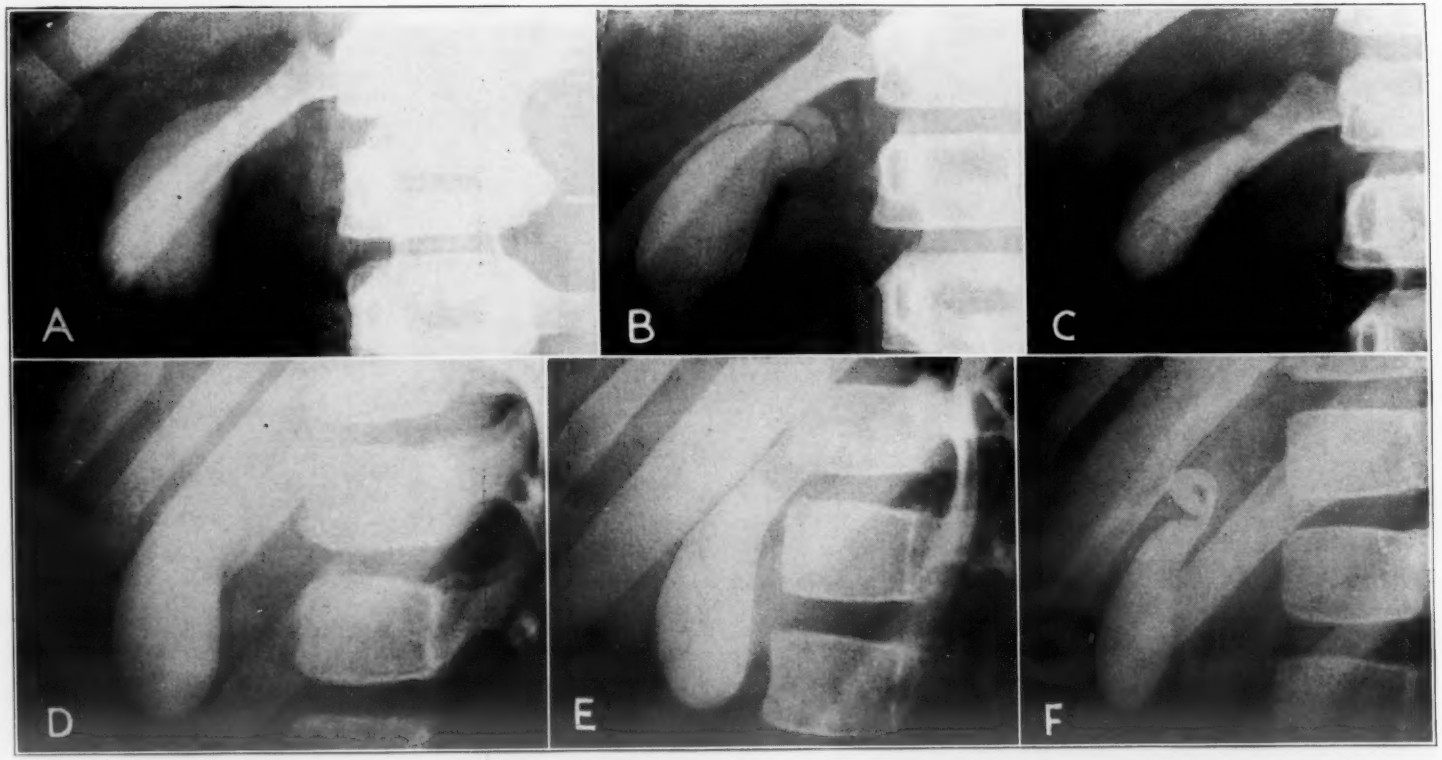

Fig. 2 (C. C., 10 year old girl).—Comparative roentgenographic views of the gallbladder. *A* shows the gallbladder, with the patient in the prone position, one and a half minutes after the eating of egg yolk; *B*, seven minutes, and *C*, twenty minutes after eating. *D* shows the gallbladder, with the patient in the side position, two and a half minutes after eating; *E*, eight and a half minutes, and *F*, twenty-one minutes after eating.

VISUALIZATION OF THE GALLBLADDER IN CHILDREN

Early in these studies it became apparent that the cystic duct and all parts of the contracting gallbladder could be readily visualized in such thin subjects as children. Eventually this condition was realized in three fourths of the twenty-eight cases. Tracings of the more striking cholecystograms are shown in figure 1. Under the most favorable circumstances (eight cases) the iodized bile outlined the cystic duct as early as eight minutes after the ingestion of food (in one case, M. S., it was visualized in six minutes, and in one other it was visible before food, C. C.). This is consistent with previous findings, namely, that in young adults the soonest that bile from the gallbladder may be aspirated from the duodenum is seven minutes after a glass of egg yolk has been swallowed.[3]

Considerable variation was observed in the shape of different gallbladders. In the majority of cases, as observed in the prone view of the subject, the common axis of the fundus, body and infundibulum constituted a straight line or a gentle curve upward to the left. But in some instances the body and the infundibulum were separated by a marked incisure or bend (figs. 1 and 4). Apparently the neck always forms an acute angle with the infundibulum. As the evacuation of bile continues, the parts of such convoluted gallbladders tend to uncoil, disclosing the detailed shape of each part. In a number of cases the cystic duct could be differentiated into pars convoluta and pars glabra—the spiral valvula of the former showing with remarkable clearness (figs. 1 and 4).

These observations suggested the idea of making roentgenograms of the children from the left side in order to secure information concerning anteroposterior relations. In adults the density of the body on side view is so great as usually to prevent the optical differentiation of the dye, but lateral views proved feasible in children with unusually dense shadows, so that for the first time it has been possible to reconstruct the gallbladder of the living patient in three dimensions (figs. 2 to 4).

Study of eight cases, each with successful roentgenograms from both angles, indicates that in the prone position the gallbladder usually slopes forward (from above downward), forming an acute angle of less than 30 degrees with the adjacent portion of the spine.

The lateral views also showed that the infundibulum bends to the left (in passing upward) within the plane of the postero-inferior surface of the liver, but that it does not bend anteriorly or posteriorly (fig. 4).

3. Boyden, E. A., and Birch, C. L.: Response of Gall-Bladder to Substances Injected into the Duodenum, Am. J. Physiol. **92**:287, 1930.

The neck of the bladder, however, bends both to the right and forward (figs. 2 and 4) as it extends upward.

Two conclusions may be drawn from these observations: (1) that the computation of volumes made from prone views are frequently based on foreshortened images and therefore provide an underestimate of absolute volume, and (2) that since the shape of the gallbladder in cross-section varies with the individual—being round in some patients and in others compressed either from side to side or anteroposteriorly—the absolute volume cannot be successfully computed in the absence of data concerning both diameters.

Advocates of the theory of passive emptying of the gallbladder by means of external pressure and not by the action of its intrinsic musculature have made much of the possibility that cholecystograms restricted to one plane offer incomplete evidence as to the extent and rate of emptying of the viscus. But examination of figure 5 shows clearly that

TABLE 1.—*The Position of the Gallbladder in Eight Children*

Case	Range of Position Degrees	Average Angle, Degrees
S. Z.	(Parallel to spine)	(None)
C. C. (fig. 2)	7.5 to 26.0	16.75
R. P. (fig. 4)	(None)	17.0
W. S.	13.0 to 23.5	18.25
A. L.	18.0 to 25.0	21.5
Cl. B. (fig. 3)	18.0 to 28.5	23.25
Ch. B. (fig. 4)	22.0 to 25.0	23.25
M. B. (erect posture)	27.5 to 31.0	29.25

whether the contracting gallbladder is or is not quite round in cross-section, the successive contours of either view (taken by itself) are being reduced proportionally. Therefore, in accordance with the theorem that the volume of any two similar solids is proportional to the cube of any two similar lines, it may be assumed that the percentage loss of volume, i. e., the rate of emptying, would be virtually the same whichever view of the gallbladder is being used for computation; and such has proved to be the case (fig. 5).[4]

The absolute volume, on the contrary, will lie somewhere between the computations made from prone and side views—each, by the requirements of the method, being based on the assumption that the gallbladder is round in cross-section—and can be estimated only approximately. But, as pointed out in previous articles, the important information from the standpoint of the analysis of function is the relative decrease in

4. Obviously this would not be true if the gallbladder were emptied by such malforming agencies as pressure of food in the stomach or duodenum, or the peristaltic action of either organ, as has recently been advocated by Newcomer, Newcomer and Conyers (Radiology **17**:317, 1931). Boyden (Am. J. Roentgenol. **27**:423, 1932) has discussed this ancient theory.

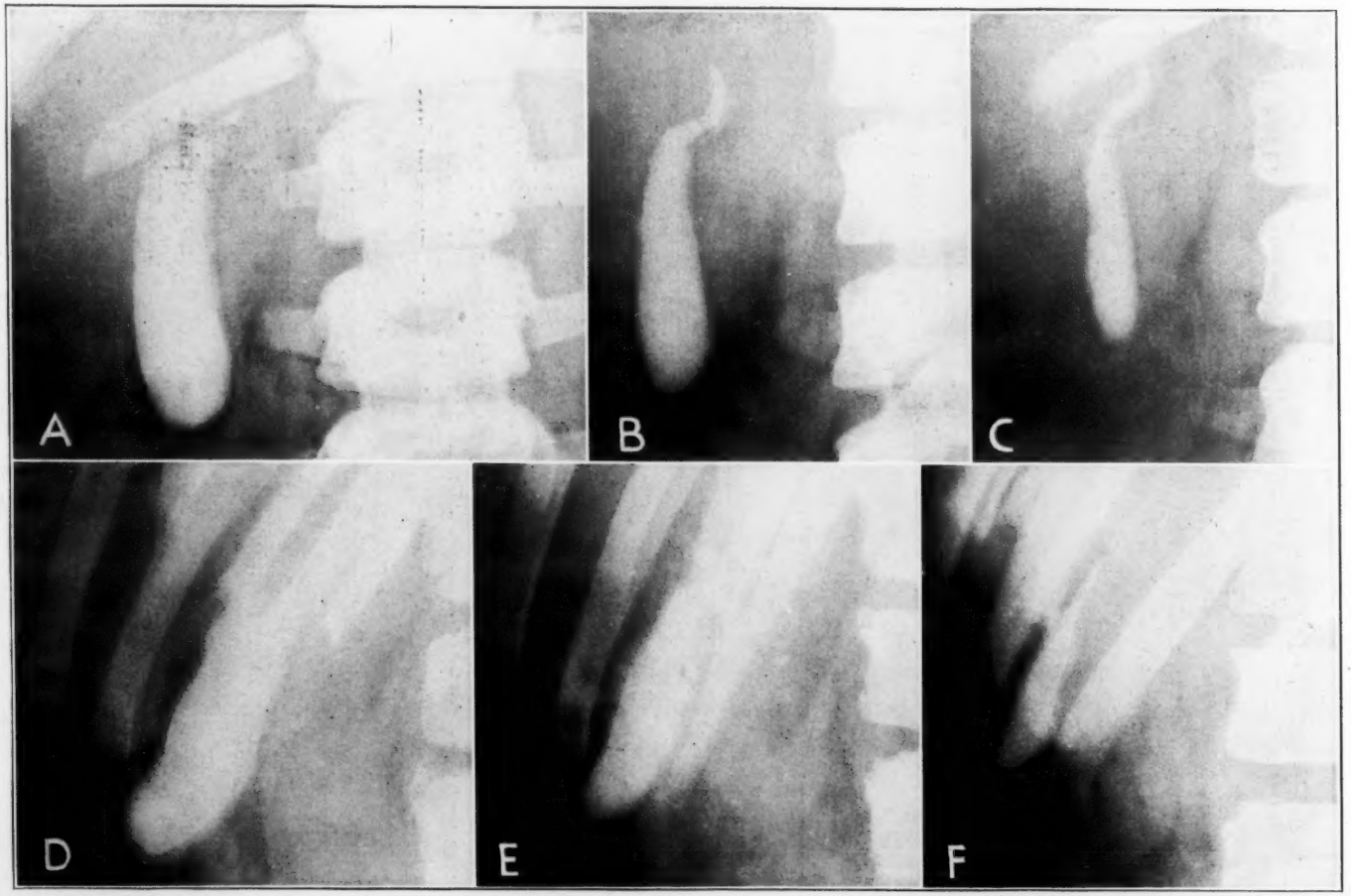

Fig. 3 (Cl. B., 10 year old boy).—Roentgenograms *A*, *B* and *C* show the gallbladder, with the patient in the prone position, one and a half, twelve and thirty minutes, respectively, after the eating of egg yolk; *D*, *E* and *F* show the gallbladder, with the patient in the side position, three, thirteen and thirty-one minutes, respectively, after eating.

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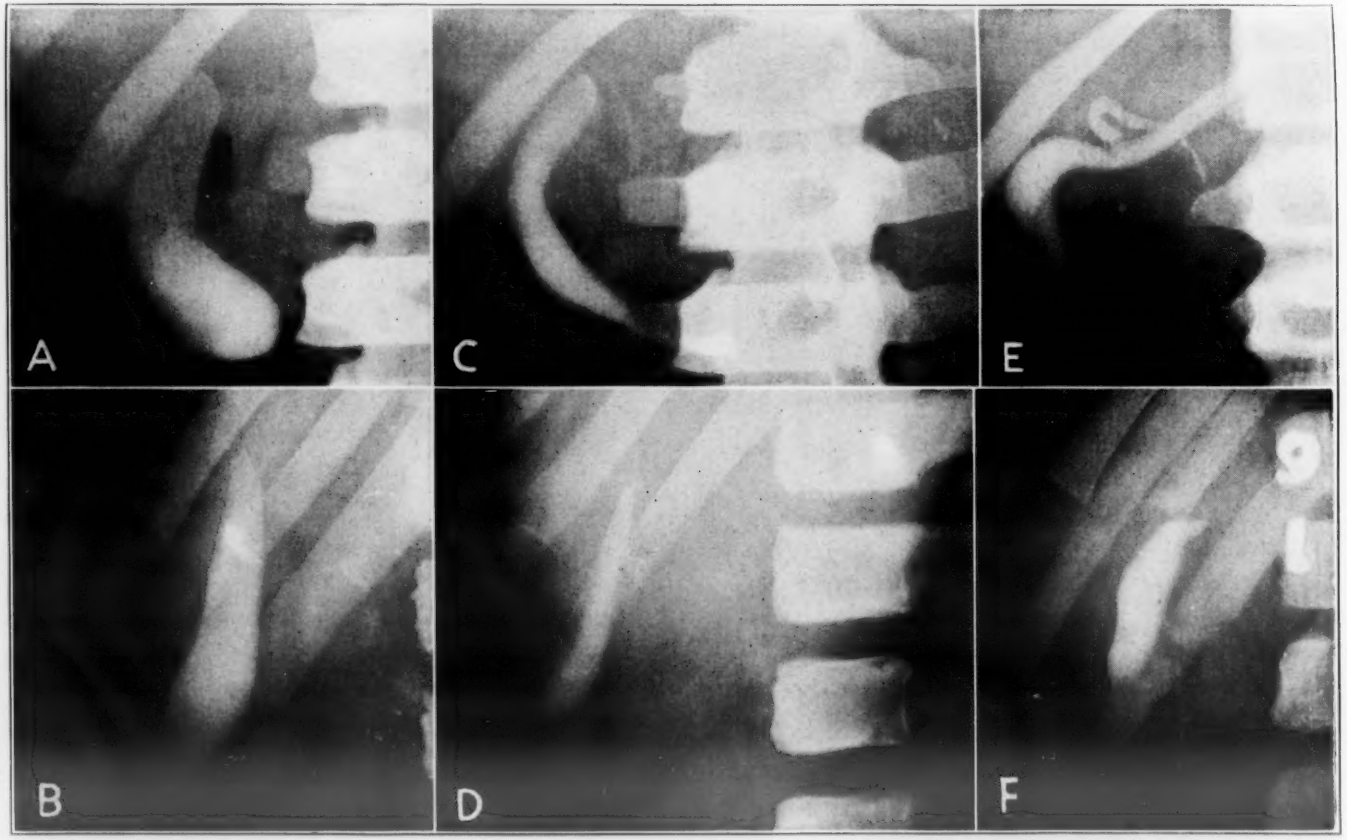

Fig. 4.—Roentgenograms showing two bizarre types of gallbladder. *A* shows the gallbladder of a boy, Ch. B., prone, before the eating of egg yolk; *B*, on side, six minutes, *C*, thirty-six minutes, and *D*, on side, thirty-seven minutes after eating; *E* shows the gallbladder of a girl, R. P., prone, sixty-five minutes after eating, and *F*, on side, sixty-nine minutes after eating.

volume, and this, as already indicated, can be obtained from cholecystograms made in either plane of the body. Since the prone view is more easily obtained and is the one which has been used in studying the gallbladder in adults, this view has been selected for analysis of the evacuation of the gallbladder in children.

THE RATE OF EMPTYING IN CHILDREN

General Observations.—In the preceding studies [2] made on young adults the computed volumes were presented in two forms: first, as graphs of individual cases, and second, as tables comparing the amount of bile discharged from the gallbladder fifteen, thirty and forty-five minutes after a standard meal of egg yolk and cream.[5]

In the present analysis of data the second method has been modified, but the first has been retained. Graphs of the gallbladder of a child drawn to the same scale as before are shown in figures 6 and 7. In general the curves of emptying are much like those of the adult, except that the initial volumes are not so large (Boyden,[2] figs. 3 and 4). As before, the principal period of discharge occurred within the first forty minutes after the ingestion of food. The "two-minute pause" (a characteristic delay in emptying, between two and four minutes after the meal) also appeared in children (A. L., D. D. and G. D., fig. 6), but its incidence could not be studied satisfactorily owing to the fact that in many children the side views of the gallbladder were interpolated at this point. Also, as before, a reversal of the usual reaction to food was sometimes encountered, as instances of gallbladders that relaxed before contracting, thereby appearing temporarily larger in volume than before the egg yolk was ingested (M. B. and L. M., fig. 7).

Indeed, it was this initial variation in tonus that led to the modification of the second method of studying the rate of emptying, namely, the determination of the percentage of bile discharged at intervals after a meal. In each series the cholecystogram was selected as unity which first showed the gallbladder in tonus, either just before or just after food was taken. Usually the two minute reading provided the truest estimate. Considering this as unity, the loss of volume (per cent) was then calculated for each succeeding cholecystogram. The more impor-

5. In these earlier studies a mixture of the yolk of five eggs and cream was used to insure complete emptying of the gallbladder. Subsequently it was noted that the yolk of only one egg introduced directly into the duodenum by a Rehfuss tube was sufficient to induce a maximum discharge during the first forty minutes (fig. 13 in Boyden [2]). Accordingly, when given by mouth, the yolks of three eggs were considered ample for children and four for adults. Milk and cream are of use merely as a palatable medium, since their activation of the gallbladder is inferior to that of egg yolk (fig. 12 in Boyden [2]).

TABLE 2.—*Emptying of the Gallbladder in Children After Ingestion of the Yolks of Three Eggs Mixed with Milk*

Case	Age	Weight, Kg.	Cause of Hospitalization	Volume at Intervals After Eating: 2 Minutes,* Cc.	8 Minutes Cc.	8 Minutes Per Cent Loss	12 Minutes Cc.	12 Minutes Per Cent Loss	20 Minutes Cc.	20 Minutes Per Cent Loss	30 Minutes Cc.	30 Minutes Per Cent Loss	40 minutes Cc.	40 minutes Per Cent Loss
A. 12 Girls														
R. P.	6.5	15.0	Icterus	8.06 (0 min.)	6.56	18.6	5.92	26.6	4.75	41.1	3.32	58.8	3.0	62.8
B. P.	7.0	19.4	Congenital syphilis of the joints	9.9	8.05	18.7	6.8	31.3	34.4	65.3	0.86	91.3	0.0	100.0
M. B.	7.5	19.3	Xeroderma pigmentosum	14.06	10.18	27.6	8.4	40.3	5.31	62.2	4.53	67.8	4.43	68.5
M. B.[2]	7.6	21.8	Chronic eczema	20.6	13.5	34.5	9.58	53.5	7.53	63.4	5.9	71.3	4.13	79.9
A. S.	8.0	20.5	Facial burn	17.94	13.2	26.4	9.18	48.8	6.36	64.6	3.1	82.7	2.7	84.9
L. S.	8.3	21.6	Migraine	6.3	6.31	....	(8.35)*	....	5.57	11.6	3.7	41.3	2.29	63.7
L. M.	8.7	21.1	Abdominal pain, constipation	8.53	7.7	9.7	6.4	25.0	4.59	46.2	4.1	51.9	3.61	57.7
Cl. C.	9.6	25.4	Chorea minor	19.35	15.1	22.0	10.9	43.7	6.36	67.1	4.5	76.7	2.92	84.9
V. V.	10.3	25.9	After appendectomy	13.2	8.9	32.6	6.0	54.6	2.0	84.8	1.8	86.3	1.0	92.4
A. T.	10.8	?	Osteomyelitis of the leg	10.61	8.88	16.3	6.46	39.1	3.96	62.7	3.87	63.5	3.61	66.0
V. B.	11.0	33.9	Infection of the upper respiratory tract	20.09 (0 min).	16.7	16.9	15.7	21.9	12.4	38.3	8.18	59.3	5.45	72.9
D. W.	11.4	30.9	Harelip, cleft palate	13.2	12.86	2.6	9.04	31.5	5.74	56.5	2.72	79.4	1.29	90.2
						225.9		416.3		663.8		830.5		923.9
Mean per cent loss in 12 girls						18.8		34.7		55.3		69.2		77.0
B. 16 Boys														
W. S.	6+	19.9	Trauma of one eye	11.64	4.2	63.9	2.0	82.8	1.2	89.7	0.5	95.7	0.3	97.4
Ch. B.	6.2	21.9	Osteomyelitis of the arm	11.4	7.1	37.7	4.9	57.0	4.0	64.9	3.1	72.8	1.5	86.8
W. McC.	7.5	24.9	Peripheral neuritis, lead poisoning	20.66	15.2	26.4	11.1	46.3	7.98	61.4	6.8	67.1	6.1	70.5
J. S.	8.5	26.2	Epilepsy	5.31 (3 min.)	4.0	24.7	2.5	52.9	1.26	76.3	0.8	84.9	...	....
A. L.	8.7	31.4	Osteomyelitis of the femurs	23.4	15.35	34.4	10.8	53.8	6.93	70.4	3.87	83.4	2.62	88.8
W. McM.	8.7	21.4	Colles' fracture	13.39	9.33	30.3	4.3	67.9	2.7	79.8	0.8	94.0	...	....
R. G.	8.9	30.8	Radical mastoidectomy	11.19 (0 min.)	9.9	11.5	9.2	17.8	6.31	43.6	3.7	66.9	3.0	73.2
G. D.	9.0	23.5	Arthrodesis (postpoliomyelitic)	21.33	20.33	4.7	16.07	24.7	8.61	59.6	7.31	65.7	6.4	70.0
R. H.	9.4	22.3	Progressive muscular dystrophy of legs	14.06 (0 min.)	4.42	68.6	2.8	80.1	2.0	85.8	1.33	90.5	...	....
H. B.	9.7	21.9	Mastoidectomy	11.31	5.02	55.6	3.4	69.9	1.72	84.8	1.86	83.6	1.15	89.8
Cl. B.	10.2	28.0	Osteomyelitis of the tibia	13.49 (1.5 min.)	7.75	42.6	5.59	58.6	4.3	68.1	2.3	82.9	1.8	86.7
S. Z.	10.3	26.4	Spastic colon (?)	14.5	13.2	9.0	11.62	19.9	8.78	39.4	5.63	61.2	4.1	71.7
Z. J.	10.5	25.4	Cataract	8.74	6.17	29.4	3.44	60.6	2.1	76.0	1.2	86.3	1.2	86.3
E. W.	10.5	28.8	Asthma	23.3	16.5	29.2	13.31	42.9	8.4	63.9	5.74	75.4	4.62	80.2
E. T.	10.7	31.8	Osteomyelitis of the skull	16.93 (0 min.)	7.74	54.3	3.6	78.7	2.8	83.5	....	....	....	....
D. D.	11.3	29.9	Orbital tumor	7.75	6.72	13.3	4.9	36.8	2.0	74.1	1.63	79.0	1.32	83.0
						535.6		850.7		1,121.3		1,189.4		984.4
Mean per cent loss in 16 boys						33.5		53.2		70.1		79.3		82.0
Mean per cent loss in 28 boys and girls						27.2		45.2		63.8		74.8		79.5

* Considered as 100 per cent; substitute readings are noted in parenthesis.

tant readings have been recorded in table 2. The summary shows that, on the average, the gallbladders of the twenty-eight children discharged approximately 27 per cent of their contents in the first eight minutes after the ingestion of egg yolk, 45 per cent after twelve minutes, 64

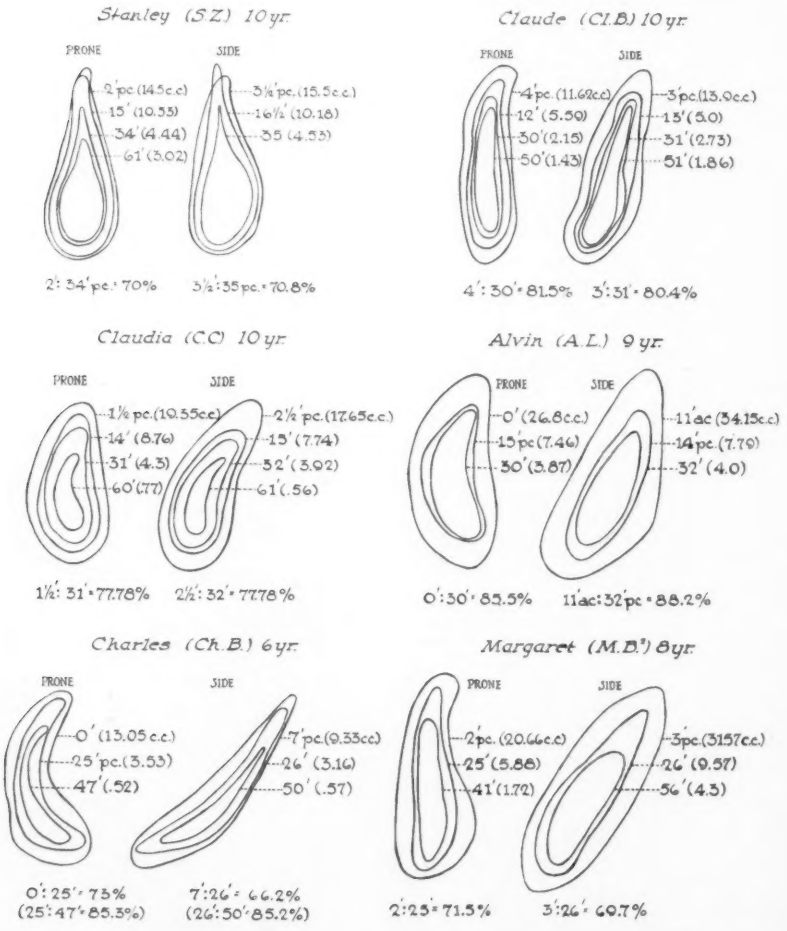

Fig. 5.—Tracings of cholecystograms showing the reduction of volume in six children after a meal of egg yolk. In each case roentgenograms were made of the same person in the prone position and lying on the right side. The leaders attached to the outlines indicate minutes before a meal (*ac.*) or after a meal (*pc.*) and computed volume in cubic centimeters. The legends underneath indicate the loss of volume in comparable intervals of time for each view. (Original photographs of *C. C.*, *Cl. B.* and *Ch. B.* are shown, respectively, in figures 2, 3 and 4.)

per cent after twenty minutes, 75 per cent after thirty minutes and nearly 80 per cent by the end of the first forty minutes.

TABLE 3.—*Emptying of Gallbladder in Adults*

Subject	Age	Weight, Pounds	Volume at Intervals After Eating: 2 Minutes,* Cc.	8 Minutes: Cc.	8 Minutes: Per Cent Loss	12 Minutes: Cc.	12 Minutes: Per Cent Loss	20 Minutes: Cc.	20 Minutes: Per Cent Loss	30 Minutes: Cc.	30 Minutes: Per Cent Loss	40 Minutes: Cc.	40 Minutes: Per Cent Loss
A. 12 Women													
E. E.	17	106	13.57	(15.2)	....	13.43	1.04	5.17	61.9	2.91	78.6	2.58	81.0
F. E. D.	18	120	13.57	(15.2)	....	(15.2)	....	11.21	17.4	7.38	45.6	3.83	71.8
L. R. F.	21	119	35.27	29.52	16.3	22.43	36.4	14.31	59.4	10.33	70.7	8.04	77.2
K. L. L.	22	128	24.2	22.3	7.9	18.45	23.8	13.57	43.9	10.33	57.3	7.96	67.1
J. M. L.	22	130	38.38	34.69	9.6	31.73	17.3	22.14	42.3	15.95	60.8	14.76	61.6
H. H. K.	23	190	18.2	17.71	2.7	9.6	47.3	5.5	69.8	4.6	74.7	4.13	77.3
A. H. H.	24	160	42.51	29.07	31.6	21.99	48.3	14.42	66.1	11.21	73.6	9.74	77.1
S. M. O.	24	122	31.0 (4 min.)	26.71	13.8	18.3	41.0	13.58	56.2	11.51	62.9	11.07	64.3
H. H. S.	28	155	15.78 (0 min.)	(21.7)	....	(18.0)	....	(18.59)	....	15.75	0.2	11.36	28.0
C. L. B.	29	115	17.85	10.48	41.3	8.26	53.7	4.16	76.7	2.36	86.8	2.36	86.8
C. H. S.	29	110	17.71	7.23	59.2	1.92	89.2	1.35	92.4	(3.0)	92.4	(4.0)	92.4
R. S.	34	121	18.73 (4 min.)	14.17	24.4	7.82	58.3	1.18	93.7	(2.1)	93.7	(2.1)	93.7
					206.8		416.3		679.8		797.3		878.3
Mean per cent loss in 12 women					17.2		34.7		56.7		66.4		73.2
B. 12 Men													
I. D.	18	145	40.32 (4 min.)	39.06	3.1	32.76	18.7	28.44	29.5	25.02	37.9	23.04	42.9
F. K. H.	19	155	15.75	13.59	13.7	10.80	31.4	9.63	38.9	(10.8)	38.9	7.4	53.0
J. S. L. †	21	175	25.58 (0 min.)	23.12	9.6	20.66	19.2	14.92	41.7	13.05	49.0	11.05	56.8
W. A. G. †	22	135	24.93	(25.75)	....	(28.98)	....	24.27	2.6	12.05	51.6	5.6	77.5
R. C. C. †	22	140	30.18 (0 min.)	(36.01)	....	(32.8)	....	28.52	5.5	18.79	37.74	14.2	52.9
L. J. B. †‡	22	151	54.28	38.7	28.7	30.0	44.73	16.74	69.2	(17.38)	69.2	(20.09)	69.2
R. J. B. †	22	155	33.96 (0 min.)	25.68	24.4	15.23	55.2	9.28	72.7	5.99	82.4	(6.07)	82.4
R. L. W.	24	112	24.5	17.6	28.2	13.57	44.6	11.21	54.2	(12.25)	54.2	9.0	63.3
N. A. C.	25	141	27.9	(30.7)	....	(28.89)	....	24.93	10.6	20.79	25.5	17.82	36.1
L. O. M.	26	175	27.18	20.7	23.8	15.48	43.0	8.6	68.4	5.13	81.1	3.75	86.2
N. B. B.	27	165	25.83	18.9	26.8	13.72	46.9	7.83	69.7	6.21	76.0	3.69	85.7
K. L. †	28	163	39.7	34.6	12.8	27.06	31.8	16.24	59.1	14.1	64.5	12.46	68.6
					171.1		335.53		522.1		668.0		774.6
Mean per cent loss in 12 men					14.3		28.0		43.5		55.7		64.6
Mean per cent loss in 24 adults					15.7		31.3		50.1		61.1		68.9
Mean per cent loss in 52 adults and children					21.9		38.8		57.4		68.3		74.2

* Considered as 100 per cent; substitute readings noted in parenthesis.
† New cases (after a meal of the yolks of four eggs mixed with milk; all others after the yolks of five eggs mixed with cream) based on data collected for Boyden.[2]
‡ Side view.

Possible Effect of Pathologic Condition.—Consideration of the causes for which these children were admitted to the hospital leaves the impression that the emptying time of the gallbladder is not influenced by most of the conditions listed in table 2, such as osteomyelitis (five cases), muscular weakness, various traumatic conditions and epilepsy.[6] But it may be significant that the two lowest readings in girls (62.8 and 57.7 per cent, respectively, forty minutes after the meal) occurred in children admitted for the treatment of icterus and obscure abdominal pain; that a third case of gastro-intestinal disturbance (S. Z.) gave among the three lowest readings (at forty minutes) in boys, and that a case of migraine gave the third lowest reading in girls. These findings are suggestive, yet in view of the fact that faradic stimulation of the human stomach and duodenum is not able to inhibit a gallbladder that is emptying under the influence of egg yolk[7] one should be cautious about assuming that chronic gastro-intestinal disorders retard the emptying of the gallbladder.

Age and Sex Differences.—Comparison of the mean rate of emptying of the gallbladder in twenty-eight children with that in twenty-four young adults (table 3)[8] reveals a significant difference between the two groups. As shown graphically in figure 9, only 20 per cent of the bile remains in the gallbladder of children after forty minutes of emptying (a loss of 80 per cent), whereas in adults nearly 32 per cent remains (a loss of 68 per cent). When submitted to statistical treatment (table 4 A), the differences between these means are consistently more than twice their standard error, and hence are significant. In other words, the probability ($P \times 100$) that the differences could be due to random sampling is less than one and two tenths times in a hundred.[9]

On the surface these figures seem to point merely to an age difference. But when children and adults are grouped according to sex

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6. Four cases of adult epilepsy, previously studied, failed to show any deviation of the gallbladder from normal in this disease (Boyden, E. A., and Saunders, A. M.: Duodenal Drainage of the Human Gall Bladder, Proc. Soc. Exper. Biol. & Med. **25**:458, 1928).

7. Boyden, E. A.: The Reaction of the Human Gall-Bladder to Faradic Stimulation of the Intestinal Tract, Anat. Rec. (supp.) **55**:8, 1933 (see also vol. 59, no. 4).

8. The data for adults were secured largely from healthy young medical students. The data for eighteen of the series (students in the University of Illinois) were compiled from material previously published,[2] since then recalculated with the two minute reading considered as unity. The remaining six subjects (dagger, table 3) are a new series comprising students in the University of Minnesota.

9. In ordinary statistical parlance, if a difference occurs less than five times in a hundred it is assumed that it is not due to chance. Dr. Edith Boyd supervised the statistical analyses in this article.

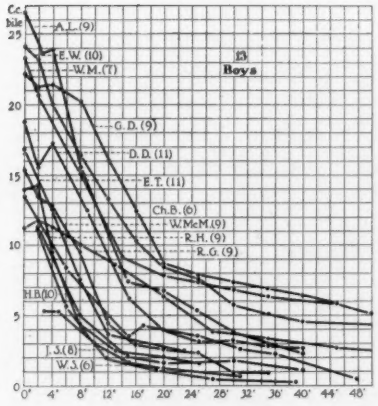


Figure 6

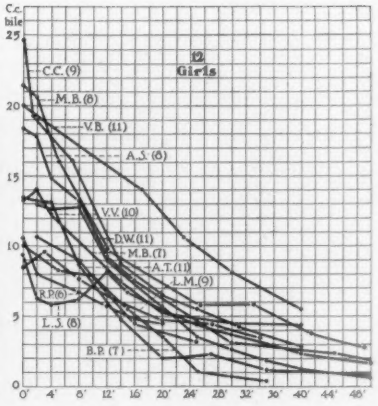


Figure 7.

Figs. 6 and 7.—Graphs for individual cases recorded in table 2, showing the change in volume of the fundus, body and infundibulum of the gallbladder in boys (fig. 6), and in girls (fig. 7), after a meal of the yolks of three eggs and milk. The abscissas indicate the minutes after the ingestion of food and the ordinates the contents of the gallbladder in cubic centimeters. All computations were made from prone views, using a method that assumes that the gallbladder is round in cross-section. While this may give an underestimate or overestimate of absolute volume, it affords an accurate estimate of the rate of emptying, since the contours of the gallbladder diminish proportionally. The volumes in D.D. have been multiplied by 2; graphs for S.Z., Cl.B. and Z.J. (table 2) have been omitted from figure 6 in order to prevent overcrowding.

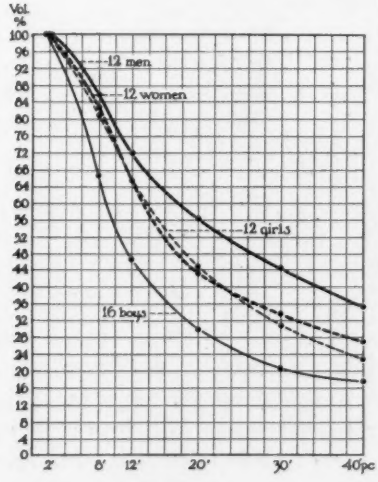


Figure 8.

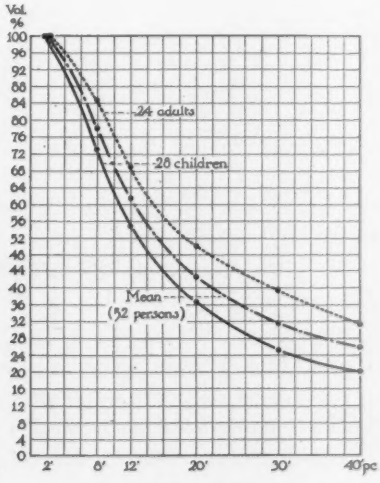


Figure 9.

Figs. 8 and 9.—Graphs showing the mean rate of emptying of the gallbladder according to age and sex. The abscissas indicate the minutes after food and the ordinates the percentage of initial volume.

(fig. 8), the striking fact appears that apparent age differences are due primarily to sex differences—to changes undergone by the male gallbladder in passing from childhood to young manhood. Thus, at the forty minute period the gallbladder of boys contains only 18 per cent of its original volume, while that of men contains 35 per cent, or nearly twice as much. The probability that these differences might be due to random sampling is only once in a thousand times (table 4 B). The

TABLE 4.—*Statistical Analyses*

Time Interval, Min.	No. of Cases	Mean and Standard Error	No. of Cases	Mean and Standard Error	Difference and Standard Error	Diff. / S. E.	Probable Error
		A. Adults	vs.	Children			
8	24	15.75 ± 3.134	28	27.20 ± 3.339	−11.45 ± 4.579	2.501	0.012
12	24	31.33 ± 4.839	28	45.25 ± 3.885	−13.92 ± 6.206	2.243	0.025
20	24	50.08 ± 5.566	28	63.75 ± 3.346	−13.67 ± 6.494	2.105	0.035
30	24	61.06 ± 4.600	27	74.81 ± 2.591	−13.75 ± 5.280	2.604	0.009
40	24	68.87 ± 3.530	24	79.51 ± 2.358	−10.64 ± 4.245	2.506	0.012
		B. Men	vs.	Boys			
8	12	14.26 ± 3.384	16	33.48 ± 4.860	−19.22 ± 5.922	3.246	0.001
12	12	27.96 ± 5.787	16	53.17 ± 5.179	−25.21 ± 7.766	3.246	0.001
20	12	43.51 ± 7.585	16	70.08 ± 3.601	−26.57 ± 8.396	3.165	0.001
30	12	55.67 ± 5.455	15	79.29 ± 2.777	−23.62 ± 6.121	3.859	0.000
40	12	64.55 ± 4.806	12	82.03 ± 2.580	−17.48 ± 5.455	3.204	0.001
		C. Girls	vs.	Women			
8	12	18.83 ± 3.125	12	17.23 ± 5.408	+1.60 ± 6.246	0.256	0.795
12	12	34.69 ± 4.465	12	34.69 ± 7.901	0 ± 9.075		
20	12	55.32 ± 5.396	12	56.65 ± 8.010	−1.33 ± 9.658	0.138	0.889
30	12	69.21 ± 4.278	12	66.44 ± 7.318	+2.77 ± 8.477	0.327	0.740
40	12	76.99 ± 3.929	12	73.19 ± 5.062	+3.80 ± 6.408	0.593	0.555
		D. Boys	vs.	Girls			
8	16	33.48 ± 4.860	12	18.83 ± 3.125	14.65 ± 5.778	2.535	0.012
12	16	53.17 ± 5.179	12	34.69 ± 4.465	18.48 ± 6.838	2.703	0.0069
20	16	70.08 ± 3.601	12	55.32 ± 5.396	14.76 ± 6.497	2.275	0.022
30	15	79.29 ± 2.777	12	69.21 ± 4.278	10.08 ± 5.100	1.976	0.048
40	12	82.03 ± 2.580	12	76.99 ± 3.929	5.04 ± 4.700	1.072	0.285
		E. Men	vs.	Women			
8	12	14.26 ± 3.384	12	17.23 ± 5.408	− 2.97 ± 6.379	0.466	0.638
12	12	27.96 ± 5.787	12	34.69 ± 7.901	− 6.73 ± 9.794	0.687	0.490
20	12	43.51 ± 7.585	12	56.65 ± 8.010	−13.14 ± 11.031	1.191	0.230
30	12	55.67 ± 5.455	12	66.44 ± 7.318	−10.77 ± 9.127	1.180	0.240
40	12	64.55 ± 4.806	12	73.19 ± 5.062	− 8.64 ± 6.980	1.238	0.211

rate of evacuation of the female gallbladder, on the contrary, remains virtually unchanged (fig. 8), there being no significant difference in the emptying time of girls and women (table 4 C).

The cause of the slowing of evacuation of the male gallbladder is not obvious. As one contemplates the slowness with which certain adult male gallbladders begin to discharge bile and the speed they may subsequently develop as contraction proceeds, one gains the impression that activity of the gallbladder is merely a manifestation of forces acting in the upper portion of the intestinal tract; that is, that sex differences in the rate of evacuation of the gallbladder are due primarily to sex differences in the upper end of the small intestine—differences in the rate of absorption of food, in the rate of formation of the hormone of

the gallbladder, etc.—or to differences in the motility of the upper tract and the regulatory apparatus at the end of the common bile duct.

Finally, table 4 D indicates significant differences between the emptying of the biliary vesicle in boys and in girls, but not, at first glance, between that of men and women (table 4 E). It is believed, however, that the consistent differences between the means of the two adult groups may indicate that larger samples would probably show a sex difference.[10]

CONCLUSIONS

Cholecystograms of children, made at successive intervals after a standard meal of egg yolk, frequently permit visualization of the cystic duct, spiral valve, common bile duct and all parts of the gallbladder, thus providing new information concerning the position of this organ in the living subject.

Cholecystograms made with the child first lying prone and then on its right side demonstrate that the frontal and sagittal diameters of the gallbladder diminish proportionally after ingestion of food. Either view may, therefore, be used for estimating the rate of evacuation of the viscus.

A comparison of the rate of emptying of the gallbladder in twenty-eight children and twenty-four young adults reveals a reversal of sex differences owing to progressive slowing of the rate of discharge of the gallbladder of boys as they pass from the period of childhood to youth.[6] It is believed that these differences are to be interpreted primarily on the basis of changes taking place in the upper portion of the intestinal tract.

10. Six additional cases in men—the first series in which the volumes of the gallbladder were ever computed—revealed a similar slowness of emptying. Unfortunately these early pictures were taken at only fifteen minute intervals and so could not be fitted to the data in table 3. However, they showed a consistent reaction from medical students in three sections of the country (Boyden, E. A.: A Study of the Behavior of the Human Gall-Bladder in Response to the Ingestion of Food; Together with Some Observations on the Mechanism of the Expulsion of Bile in Experimental Animals, Anat. Rec. **33**:201, 1926).

Case Reports

RETROCECAL GANGRENOUS APPENDICITIS

COMPLICATED BY SUBDIAPHRAGMATIC ABSCESS, EMPYEMA, ABSCESS IN THE LUNG WITH BRONCHIAL FISTULA AND FECAL FISTULA, WITH OPERATIONS AND RECOVERY

JACOB L. STEIN, M.D.
AND
WILLIAM LEON WOLFSON, M.D.
BROOKLYN

Retrocecal gangrenous appendicitis is not rare. This case is reported because of its unusual complications and bacterial origin, the interesting roentgenographic observations, and the fact that complete recovery followed operations in what appeared to be a hopeless situation.

REPORT OF A CASE

History.—A boy, aged 5½ years, was admitted on Feb. 20, 1933, with the complaint of pain in the lower right portion of the abdomen.

His illness commenced three days previously, when he began to suffer from abdominal pain in the right lower portion, associated with slight fever. On the following day his condition was much improved, and he was allowed out of bed. On the day of admission he still complained of occasional cramps in the right lower quadrant.

On the day of admission the evening temperature was 103 F., the pulse rate 90 and the respiratory rate, 26. Physical examination revealed no abnormality except slight tenderness and rigidity in the right lower quadrant, tenderness over the region of the kidneys posteriorly and rebound tenderness. There was no evidence of a mass; rectal examination revealed no abnormalities. The white blood cell count was 24,000, with 88 per cent polymorphonuclears. The diagnosis was acute suppurative retrocecal appendicitis.

First Operation.—An operation was performed immediately. The McBurney muscle-splitting incision was made on the right side of the abdomen. This was started far to the right side, almost in the flank, overlying a mass which could be felt after anesthesia was administered, but not before.

An abscess caused by a ruptured appendix was found. It contained a large quantity of thick, malodorous, grayish pus. The abscess was drained; no attempt was made to remove or disturb the appendix. Three cigaret drains were inserted into the cavity. The pus yielded a pure culture of Bacillus mucosus-capsulatus (Friedländer's bacillus).

From the Pediatric and Surgical Departments, the Jewish Hospital of Brooklyn.

The child responded favorably to the operation. He did not vomit, and the wound drained freely. However, fever continued unabated, ranging from 100 to 104 F., with only slight remissions in the morning.

On the afternoon of February 25, the child became irritable, and there was a sharp rise of 3 degrees in the temperature, associated with a pulse rate of 156 and a respiratory rate of 42. The right lung from the midcapsular region to the base was dull on percussion and almost flat at the base. The breathing sounds

Fig. 1.—Roentgenogram of the chest on February 27. The diaphragm is definitely raised on the right. There is a collection of fluid beneath it, with air present, so that a definite fluid level can be demonstrated.

were tubular in the intercapsular region and suppressed at the base. There was tenderness over the lower ribs on the right side posteriorly and in the upper abdominal quadrant on the right anteriorly.

A roentgenogram showed definite elevation of the right side of the diaphragm. It revealed a collection of fluid beneath the diaphragm, with air present, so that a definite fluid level could be demonstrated.

In view of the operative condition of retrocecal appendicitis and the physical and roentgenographic findings, a tentative diagnosis of subphrenic abscess was made.

On the three following days there was some abatement of fever, with the pulse and respiratory rates falling in proportion. On March 1, however, the temperature began to rise steadily, reaching 104 F. on the afternoon of March 2 and 105 F. on the afternoon of March 3. The respiratory rate became disproportionately rapid, reaching 54 on March 2 and 68 on March 5.

Examination of the chest on March 2 revealed that the amount of air immediately beneath the diaphragm on the right side had increased. A fluid level could still be demonstrated. Some infiltration extending from the root of the right lung toward the periphery was observed just above the diaphragmatic level. The white blood cell count was 36,400, with 91 per cent polymorphonuclears. Figure 2 shows the roentgen findings.

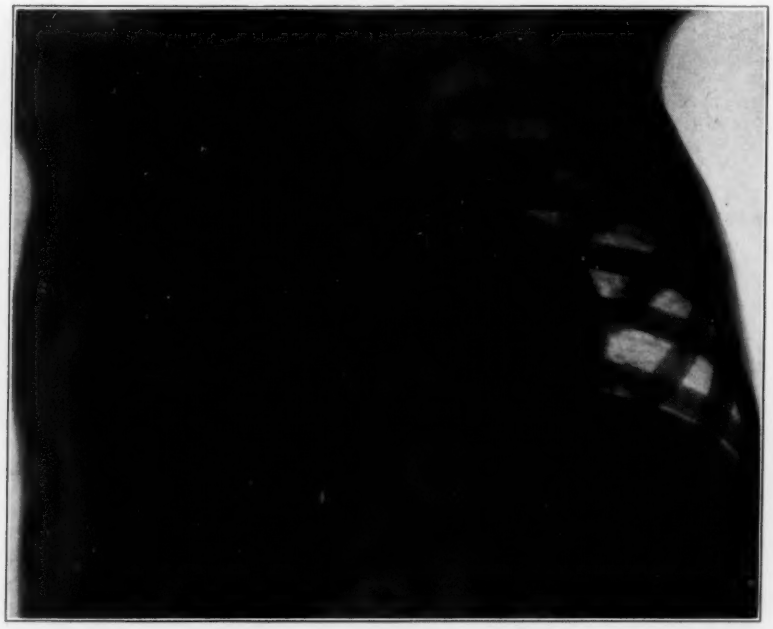


Fig. 2.—Appearance of the chest on March 2. The amount of air immediately beneath the diaphragm on the right side is more marked than in figure 1. A fluid level can still be demonstrated. There is some infiltration extending from the root of the right lung toward the periphery, just above the diaphragmatic level. This suggests a secondary pneumonic process.

Later, the veins on the right side of the abdomen and chest became engorged and dilated. On palpation there was a feeling of resistance in the abdomen, and a mass the size of an orange could be felt in the right upper quadrant.

Subsequent Operations; Course.—On March 3, under local anesthesia, a mid-axillary incision was made over the tenth rib. A section of the rib 2½ inches (62.23 cm.) in length was resected supracostally. Through this gap and in the upper part of the wound, the parietal periosteum was sewed to the diaphragm, catching the parietal and visceral layers of the pleura between these structures. This sealed the pleural cavity, thereby avoiding the soiling and suction of an open pleural wound.

Next, a transverse incision was made in the lower part of the exposed subcostal periosteum and carried through both layers of the pleura to the diaphragm. The diaphragm was incised transversely. An enormous quantity (1,000 cc.) of grayish, malodorous pus was evacuated from below the diaphragm. It was similar to that previously found in the appendical abscess. Culture, however, yielded Salmonella morgani, type 1.

The child rallied from the operation, but the temperature and the pulse and respiratory rates continued to be high. Continuous intravenous infusion of physiologic solution of sodium chloride was resorted to. On March 4 there was tympany over the right side of the chest, with amphoric breathing and dulness over the left upper portion of the chest anteriorly.

On March 5, edema of the face, especially over the eyes, lips and forehead, was observed. Intravenous infusions were discontinued. A fecal fistula had developed at the site of the original incision. There was dull tympany over the right side of the chest, with diminished breath sounds. The heart was pushed over to the left. The white blood cell count had fallen to 22,650, with 84 per cent polymorphonuclears. The temperature and pulse rate continued to be high, with the respiratory rate disproportionately rapid.

On March 6, in view of the continued fever and physical signs pointing to empyema, a needle was inserted through the chest wall posteriorly, and 30 cc. of foul-smelling pus was aspirated. Because of the patient's serious condition, operation was deferred, and an attempt was made to drain the chest by aspiration. On March 8, 100 cc. of thick pus was aspirated from the right side of the chest. Stimulation became imperative.

On March 10, closed thoracotomy was performed to relieve the empyema. A large amount of purulent material was obtained. A rubber drain was inserted in the region of the ninth rib. The child's condition was somewhat improved by the operation. Dyspnea was not so marked, and the heart receded a little to the right. The breath sounds heard anteriorly indicated reexpansion of the collapsed lung.

In spite of improvement in the pleural condition, as demonstrated by physical examination and roentgenographic study, the temperature and pulse rate continued to be elevated without remission and the respiratory rate was disproportionately rapid.

On April 3, after the site of the subdiaphragmatic abscess was probed and an attempt was made to perform aspiration on the right side of the chest anteriorly, there was a sudden rise of temperature with increased rapidity of respiration. There was a slight cough, and large quantities of purulent sputum were raised.

The right side of the chest was dull from the third rib anteriorly to the base of the lung in the axillary line. There was flatness on percussion from the middle of the axilla to the base. Breath sounds were suppressed over these areas, and occasional fine râles were heard. Posteriorly the percussion note was dull down to the angle of the scapula and flat from there to the base. Breath sounds in this area of flatness were frankly tubular. Occasional subcrepitant râles were heard at the angle of the scapula.

The condition was believed to be a pyopneumothorax communicating with a bronchus, thereby accounting for the profuse purulent expectoration (from 1 to 2 ounces [28 to 56 Gm.] a day). The possibility of a complicating pulmonary abscess with perforation into the bronchus was also considered. Because of marked cyanosis and dyspnea, an attempt was made to use the Drinker respirator to reexpand the partially collapsed lung, but since the machine could not be operated

faster than 30 per minute and the child was breathing over 50, it had to be abandoned.

With open air, sunlight, forced fluids and ultraviolet irradiation the patient began to improve rapidly. The temperature gradually diminished and after several weeks reached normal. The pulse and respiratory rates, however, continued to be disproportionately high.

Examination on April 17 showed considerable improvement. The child appeared happy, and was comfortable when sitting up in bed. There was slight dyspnea

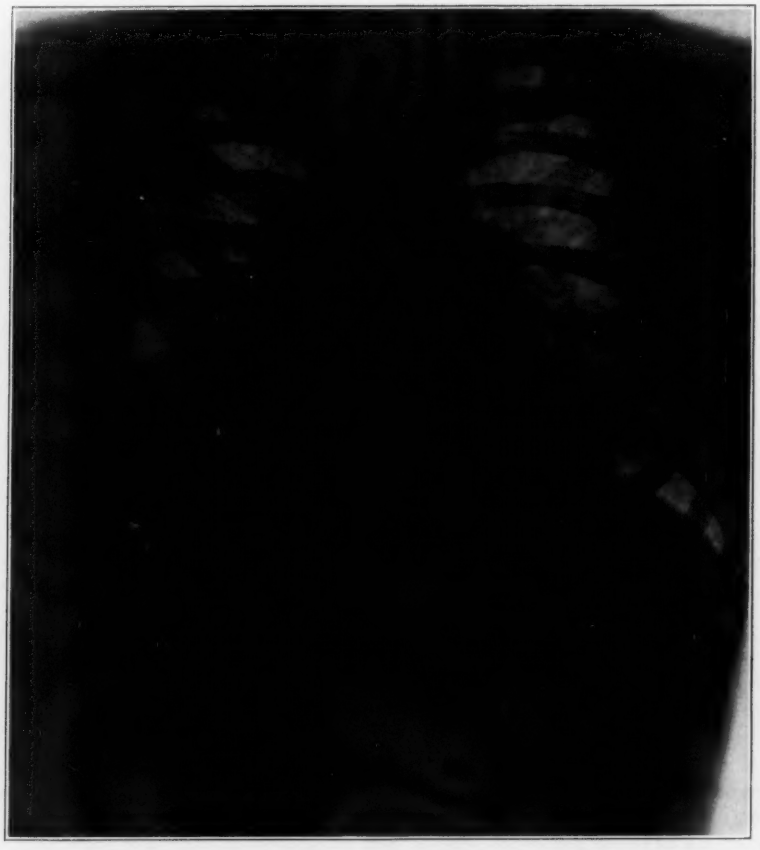


Fig. 3.—Roentgenogram of the chest on June 13. It shows a residual thickening in the right axilla at about the level of the sixth and seventh intercostal spaces posteriorly. Other than this, both lung fields are clear. The diaphragmatic cusps are smooth, and both costophrenic spaces are clear. Diaphragmatic mobility is unimpeded. The diagnosis is residual pleural thickening.

on exertion. The thoracotomy and subdiaphragmatic wounds had healed, but there was still a slight discharge from the appendical wound. The boy was still coughing up thick, purulent material. Physical examination gave evidence of residual exudate at the base of the right lung. The condition at this time was diagnosed as abscess of the lung still draining through the bronchus which it had penetrated.

There was, in addition, an abscess of the left buttock, which was incised, with the evacuation of considerable pus.

On April 27, improvement was so far advanced that the child was discharged from the hospital, and was sent to the country for six weeks' convalescence.

He returned for examination on June 13. He looked healthy and had gained 15 pounds (6.8 Kg.). All the wounds had healed completely, and there was no expectoration.

A roentgenogram taken at this time disclosed residual thickening in the right axilla at about the level of the sixth and seventh intercostal spaces posteriorly. Other than this, both lung fields were clear. The diaphragmatic cusps were smooth, and both costophrenic spaces were clear. Diaphragmatic mobility was unimpeded.

Laboratory Observations.—Reference has already been made to the blood counts. The complete observations are given in the table.

Blood Counts During the Entire Illness

Date	White Blood Cells, per C. Mm.	Polymorphonuclears, per Cent	Red Blood Cells, per C. Mm.	Hemoglobin Content, per Cent
2/20	24,000	88	5,800,000	85
2/26	26,500	82	5,840,000	80
3/3	36,400	91	6,210,000	68
3/5	22,650	84	5,150,000	61
3/11	19,500	72	3,820,000	58
3/21	26,000	62	2,550,000	56
3/28	24,750	65	3,480,000	58
4/6	38,400	88	4,040,000	56
4/14	31,500	82	4,500,000	68
4/22	14,600	76	4,070,000	70

As has been noted, pus from the appendical abscess contained B. mucosus-capsulatus (Friedländer's bacillus). S. morgani, type I, was grown on culture from the pus in the subdiaphragmatic abscess. The abdominal wounds and also the sputum yielded Bacillus proteus. Repeated blood cultures were negative.

The electrocardiographic tracing showed a ventricular rate of 160 with right ventricular preponderance. It indicated a hyperactive heart.

Results of examinations of the urine were uniformly negative. The tuberculin, Schick and Dick tests gave negative results.

COMMENT

The remarkable feature of this case is the complete recovery in spite of the number and severity of the complications. It is possible that secondary infection with B. proteus may have contributed to some extent to recovery. The rapid clearing up of extensive pleural and pulmonary lesions, as shown by roentgenograms, is also of interest.

ACUTE NECROSIS OF THE LIVER

JULIAN P. PRICE, M. D.
FLORENCE, S. C.

Acute necrosis of the liver is a rare condition in children, as evidenced by the fact that Rolleston [1] found only 43 cases reported up to 1929; for that reason this case is reported in full.

REPORT OF CASE

History.—Z. C., aged 3½ years, a white girl, had a father, mother and two sisters who were living and well. Both parents denied having venereal infection. The mother had had one miscarriage, the cause of which was unknown. There was no history of chronic or recent acute illness in the immediate family. The parents were in very poor circumstances, and had always lived on a farm. The patient, as far as the mother knew, had never been sick except for an occasional cold and infrequent attacks of vomiting. She had never received medicine except an occasional dose of "salts" and "black draught." For several months before the onset she had been in excellent health and had received no drugs.

Three days before admission the child complained of feeling poorly, and the parents noticed definite jaundice. By the next day the jaundice had become marked, and she showed evidence of lassitude and anorexia. There was occasional vomiting, and she wanted to sleep all the time. The family physician who saw the child believed that he was dealing with catarrhal jaundice and treated her accordingly. Within the next two days, however, she became decidedly worse. There was stupor, punctuated at times with extreme restlessness. The vomiting ceased, but the stools became clay-colored. At this time hospital care was advised.

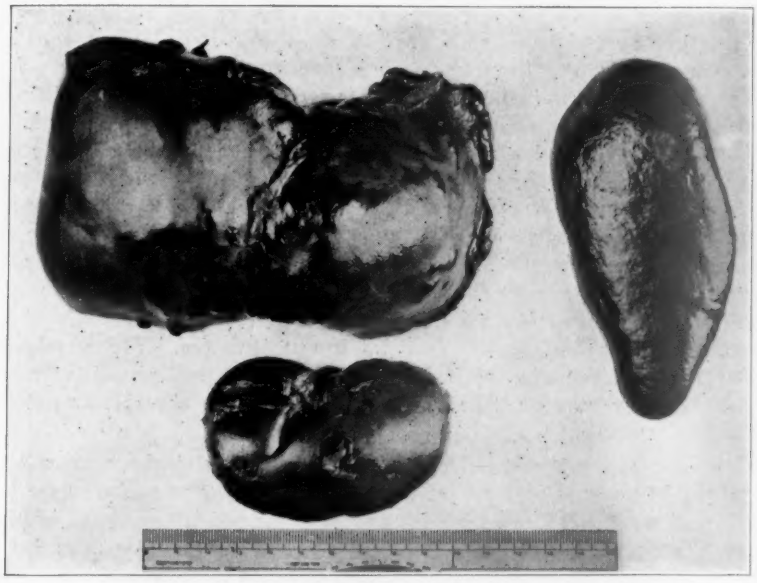
Physical Examination.—The patient lay on the bed apparently asleep except for marked generalized restlessness. Her state of general nutrition was good. The skin over the entire body was an extreme yellow, but there were no petechiae or hemorrhages. The superficial veins over the upper and lower parts of the abdomen were markedly dilated. The sclerae were of a deep icteric color. The abdomen was distended but soft. Percussion revealed a tympanitic note over the entire abdomen except in the flanks where there was slight dulness, although there was no fluid wave. There was no tenderness or spasticity, and there were no abnormal masses to be felt in the abdomen. The liver and spleen were not palpable. A careful examination of the rest of the body failed to reveal any abnormal physical or neurologic signs.

Course in Hospital.—In spite of symptomatic and supportive treatment the child grew progressively worse. The jaundice became deeper. Stupor was profound, with occasional periods of delirium which required large doses of sedatives. Distention became pronounced, and evidence of fluid in the abdomen appeared. The

1. Rolleston, H.: Diseases of the Liver, in Christian, H. A.: New York, Oxford University Press, 1932, vol. 3, p. 315.

temperature fluctuated between 100 and 102 F. The urine persistently showed bile (4 plus). A moderate leukocytosis was present throughout, with a normal differential count. The hemoglobin gradually fell to 43, and the icteric index of the blood rose to 180. The Wassermann and Kahn reactions of the blood were negative. The stools were clay-colored until the sixth day when they became black with old blood, and at the same time the child began to regurgitate blood and to have oozing of blood from the mucous membranes of the mouth. At no time were there hemorrhages into the skin, and ophthalmologic examination showed no hemorrhages into the retinas.

The stupor advanced to a profound coma, and the child died on the seventh day after admission and the tenth day after the onset of the disease.



Photograph of the liver, spleen and kidney.

Postmortem Examination.—Consent was obtained for removal of the liver. Unfortunately the autopsy was performed at night under artificial light, so that it was difficult to tell much about the yellow color. There was dilatation of all the subcutaneous blood vessels. Seven hundred fifty cubic centimeters of dark yellow fluid was removed from the abdominal cavity. The liver was tucked under the margin of the lower ribs and weighed 280 Gm. It was yellow-red, and felt soft and mushy. The capsule was wrinkled. The surface was irregular, with small yellow nodules to be felt just beneath the surface, varying in size from 0.5 to 2.5 cm. in diameter. The gallbladder was dark green and of normal size and appearance. On section the liver showed occasional dark red areas but these were interspersed with large, yellowish-ocher patches which projected above the surface. The spleen and right kidney were also removed and appeared normal, the spleen weighing 80 Gm. and the kidney 67 Gm.

The anatomic diagnosis was acute primary necrosis of the liver.

Pathologic Observations (Dr. Wiley Forbus, Professor of Pathology, School of Medicine, Duke University): The spleen measured about 10 by 5 by 3 cm. The capsule was considerably thickened and scarred, but outside of this no superficial changes of importance were seen. In a section through the spleen the malpighian bodies were recognized as large gray nodules surrounded by dark splenic pulp. Nothing abnormal could be seen except the size. The kidney measured 7 cm. from pole to pole. The pelvis contained some granular bile-stained material. The kidney seemed a little swollen. In sections no definite abnormalities could be recognized except diffuse jaundice.

The liver measured 15 cm. in transverse diameter by 8 cm. longitudinally and about 3.5 cm. in thickness. The capsule was shrunken and thickened. Projecting up from the surrounding liver tissue were irregularly shaped, bile-stained masses of what was apparently liver tissue. The gallbladder seemed about normal in size. On section it was found to contain a small amount of viscous bile. When this was removed normal gallbladder mucosa was revealed. Projecting from one of the large veins near the portal vein was a thrombus-like mass deeply stained with bile. When traced backward into the liver tissue the thrombus-like mass was found in the branches of the large vein. The impression was that there might have been an infectious process going on in connection with the central veins. The portal veins were apparently not abnormal, although in some a certain amount of the same granular material was noted. The liver tissue was composed instead of collapsed supporting connective tissue. Most of the substance had a peculiar grayish, translucent color which seemed to indicate the absence of liver tissue. Whenever liver tissue was found it was jaundiced. The greenish elevations described as projecting from the surface of the liver proved to be nodes in which hepatic cells could be recognized. These were always surrounded by collapsed liver tissue.

Microscopic Examination.—Deeply jaundiced tissue and the gray collapsed tissue could be seen in all the sections made. In the gray areas there were practically no liver cells. There were, however, a number of bile ducts, all of which appeared embedded in connective tissue which seemed to be nothing more than the normal supporting tissue of the liver which had fallen together as a result of the disappearance of the parenchyma. However, one could recognize in this tissue a certain scattering of mononuclear cells which were apparently lymphocytes. This was the only evidence of inflammation, and was probably the result of irritation of dead liver cells rather than a primary cause of their distribution. In the bile-stained areas were many liver cells, but these were in varying stages of preservation; some were necrotic, while others were filled with globules of fat indicative of progressive degeneration. A few seemed relatively normal. All the bile ducts, particularly those just distal to the capillaries, were plugged with masses of black bile pigment. No evidence of inflammation could be found in the pigmented areas except a few round cells like those in the collapsed areas without liver cells. There appeared, therefore, to be an extensive degeneration of the liver tissue, the etiology of which was entirely obscure. The process had apparently been so rapid that little or no regeneration of the liver tissue had occurred. The extensive jaundice with the obvious obstruction of the smaller bile ducts made one think at once of the possibility of a biliary obstruction with secondary degenerative changes in the liver. It was not inconceivable, however, that the collapse of the framework of the liver resulting from the distribution

of the large blocks of cells might within itself have produced obstruction of the bile ducts leading from the more or less well preserved areas of tissue. This would account for the jaundice of this tissue.

The final diagnosis was extensive necrosis of the liver of uncertain origin and possible chemical intoxication.

COMMENT

There was no suggestion of infection or chemical poison, yet the patient evidently experienced severe intoxication which directly affected the liver, producing widespread necrosis. Although the term acute yellow atrophy is usually applied to this type of condition, it is a misnomer, for there is no atrophy but, on the contrary, a widespread necrosis.

RHEUMATIC HEART DISEASE AT ONE YEAR

VINCENT E. FISCHER, M.D.
NEW YORK

A definite diagnosis of rheumatic heart disease was established after necropsy in the case reported. The occurrence of rheumatic heart disease in infancy and the prominent familial rheumatic taint appeared worthy of note.

The child was 12½ months old on admission. A review of the literature shows that reports of such cases with autopsy in patients of this age are rare. Schroeder [1] reported a case in a patient aged 20 months; Denzer [2] reported two cases in patients aged 23 months and 2 years, respectively, with mitral stenosis, which he said was of at least four, and probably of six, months' duration. Paul D. White [3] reported the condition in a patient 16½ months of age. Holt [4] in a series of 1,000 postmortem examinations found no subject under 3 years of age with endocarditis. Among 687 patients, Coombs [5] saw none under 3 years of age. Ingerman and Wilson [6] reported 2 patients less than 3 years of age in a series of 185 cases. Still [7] did not see a single patient under 2 years of age among 1,027 children with articular and cardiac rheumatism or with chorea.

The presence of acute rheumatic fever in the mother from the third to the seventh month of the fetal life of this patient is interesting and may be significant. It seems probable that intra-uterine involvement

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From the Pediatric Division, St. Vincent's Hospital.

1. Schroeder, L. C.: Observations on the Etiology and Pathology of Chorea Minor, J. A. M. A. **79**:181 (July 15) 1922.

2. Denzer, B. S.: Rheumatic Heart Disease in Children Under 2 Years of Age, J. A. M. A. **82**:1243 (April 19) 1924.

3. White, P. D.: The Incidence of Endocarditis in Earliest Childhood, Am. J. Dis. Child. **32**:536 (Oct.) 1926.

4. Holt, quoted by Bass, M. H. in Abt, J. A.: Pediatrics, New York, The Macmillan Company, 1924, vol. 4, p. 359.

5. Coombs, Carey F.: Rheumatic Heart Disease, New York, William Wood & Company, 1924.

6. Ingerman, E., and Wilson, M. G.: Rheumatism: Its Manifestations in Childhood Today, J. A. M. A. **82**:759 (March 8) 1924.

7. Still, G. F.: Common Disorders and Diseases of Childhood, New York, Oxford University Press, 1909, p. 411.

of the heart may have occurred. Poynton and Paine [8] reported a case in a child 2 days old in which diplococci were recovered from vegetations on the mitral valve, the mother having been a victim of an acute attack of rheumatism during the late months of pregnancy. The pathologic manifestations in the case reported here indicate an acute process, probably not dating from birth; but it is possible that the child was definitely stigmatized during fetal life.

REPORT OF CASE

History.—J. S. was admitted on Jan. 22, 1933, at the age of 1 year and 22 days, and died nine days after admission. The chief complaints on admission were fever, convulsions occurring two days before admission and a discharge from the right ear for twenty-two days. The present illness began four weeks before admission with the onset of high fever. Myringotomy was done on both ears and the fever subsided two days later, but pus continued to drain from the ears. Pus had ceased to drain from the left ear one week before admission, but there was still a discharge from the right ear. Two days before admission the child had two convulsions, each lasting about ten minutes and occurring about two hours apart. The temperature varied from 102 F. at the onset of the convulsions to 104 F. at the time of admission. The child vomited a small amount on one occasion. A slight cough had developed on the day of admission. No urinary symptoms were elicited.

The family history was of considerable importance. The mother and father were both Puerto Ricans. The mother had lived in New York for a period of five years. She was ill with influenza when the child was admitted. She gave a history of having her first attack of polyarthritis while pregnant with this patient. The polyarthritis occurred at about the third month of pregnancy. The arthritis was migratory and involved the knees, ankles, wrists and elbows, but was not associated with redness or swelling. The attack lasted for four months, but the patient was not seen by a physician during that time. The second attack of polyarthritis occurred five months post partum and was of one month's duration. She has been treated for heart disease for the past two years. At the present time she shows an enlarged heart and a loud, coarse, systolic murmur at the apex. The father has lived in New York for seven years. He had a definite attack of acute rheumatic fever five years ago. A sister of the patient, aged 2½ years, has complained of transient pain in the right knee for the past eleven months. Five months ago her heart appeared to be normal, but there is now a definite systolic murmur at the apex. The maternal grandmother is said to have rheumatic heart disease. The maternal grandfather is said to have rheumatism.

The child was breast fed for eight months. Cod liver oil was not given until the child was 7½ months old. Orange juice was given from the age of 4 weeks. The developmental history was normal, and the child had always been well nourished and gained weight. There was no history of previous illness of any kind. No immunologic work had been done.

Examination.—The physical examination on admission showed a well developed, well nourished child not appearing to be acutely ill, with a temperature of 104 F. The head showed prominent frontal bosses, but the anterior fontanel was closed.

8. Poynton, F. J., and Paine, A.: Researches on Rheumatism, London, J. & A. Churchill, 1913, p. 389.

The left ear showed the tympanic membrane to be bulging slightly. The right ear showed a perforated tympanic membrane from which foul pus was draining, and bulging of Shrapnell's membrane. The tonsils were large, but the pharynx was normal otherwise. There was no rigidity of the neck or palpable glands. Slight changes on percussion and fremitus changes were noted in the upper lobe of the left lung, posteriorly. The thorax was symmetrical and showed no beading of the ribs. The heart showed regular rhythm and there were no thrills or murmurs. Percussion did not reveal enlargement. Otherwise the examination gave negative results.

Fig. 1.—The heart, showing the warty, beadlike elevations located slightly above the line of closure of the mitral cusps.

Laboratory Data.—An electrocardiogram taken shortly before death showed an auricular rate of 160, a ventricular rate of 160, a Q R S interval of from 0.04 to 0.06 second, with a conduction time from auricle to ventricle of from 0.12 to 0.14 second. The interpretation was sinus rhythm. The urine on the patient's admission showed a moderate amount of albumin and casts. Subsequent examinations gave negative results. The blood chemistry showed: sugar, 119 mg. per hundred cubic centimeters; nonprotein nitrogen, 25.5, and chlorides, 546. The spinal fluid chemistry showed: sugar, 75 mg. per hundred cubic centimeters; protein, 15 and chlorides, 701. The reaction to the Schick test was positive. The tuberculin and Kahn tests were negative.

Course.—A spinal puncture, done on admission, showed the fluid clear and not under pressure, with 6 cells per cubic centimeter. The temperature ranged from

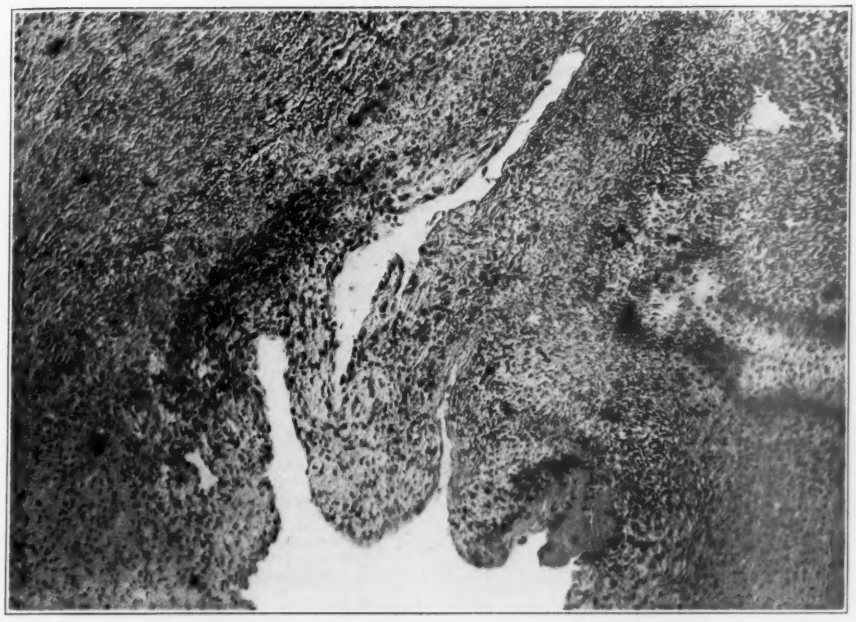

Fig. 2.—A section from the mitral valve, showing masses of platelet thrombi on the surface of the valve and proliferation of the reticular cells beneath the endothelium.

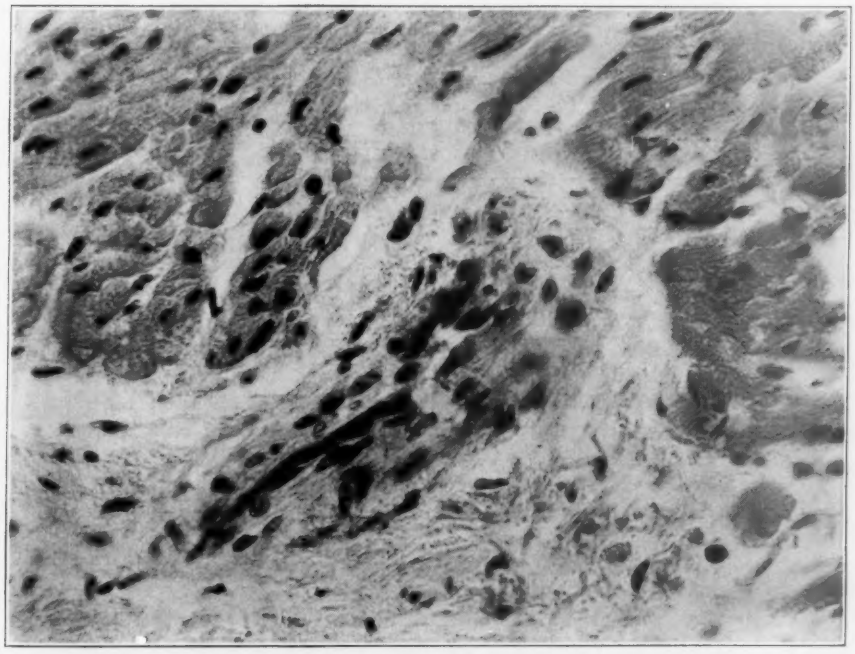

Fig. 3.—A high power photomicrograph of a section from the papillary muscle, showing Aschoff cells grouped about a blood vessel.

101 to 104 F. for four days after admission and then subsided by crisis. Repeated examinations of the heart and lungs showed only the presence of rhonchi in both lungs at this time. Four days after admission a loud, coarse, blowing systolic murmur was heard over the entire precordium, most prominent at the apex. The temperature showed practically no variations until death, four days later. Two days before death signs of consolidation were discovered in the upper lobe of the right lung. A pericardial friction rub was not heard at any time.

The diagnosis before death was chronic purulent otitis media, lobar pneumonia, congenital heart disease and mild rickets.

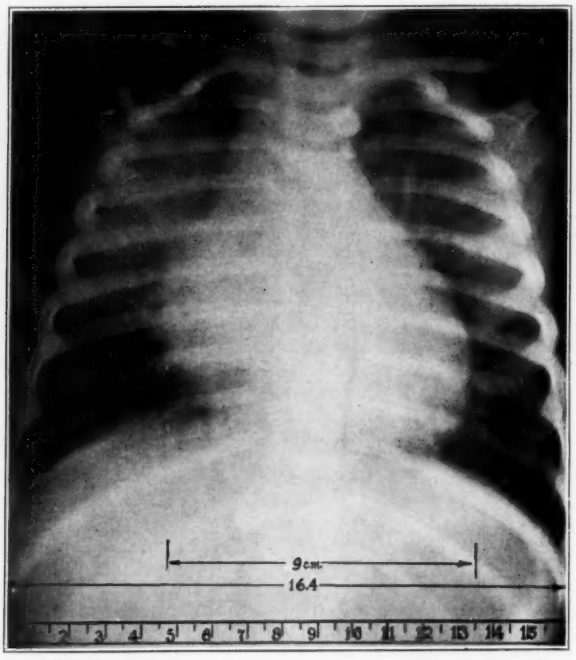

Fig. 4.—A roentgenogram (anteroposterior) of the chest, showing enlargement of the heart to the right.

Autopsy.—The autopsy was done and reported by Dr. Alexander Fraser.

The lower lobe and about one half of the upper lobe of the right lung were completely consolidated in the stage of gray hepatization. The apex of the upper lobe showed compensatory emphysema. The left lung, for the most part, showed compensatory emphysema, with passive congestion and edema of the lower part.

The heart was slightly enlarged by dilatation. The foramen ovale was patent. The mitral valve showed an even layer of warty beads running along the margin of the cusps. The aortic valve was normal, as were the coronary arteries. The myocardium was firm in consistency and of good color. There was no evidence of pericarditis. The aorta was normal.

Microscopic sections of the lungs were typical of lobar pneumonia.

Sections from the wartlike growths on the mitral valve showed an essentially proliferative change. This proliferation was of the reticular cells situated beneath the endothelium of the valves. The cells were large and in places formed a papil-

lary-like covering over the cusps. They were usually mononuclear with a large amount of cytoplasm, but occasionally there were several nuclei. In places these large cells were mixed with lymphocytes. These cells were the same as those found in so-called Aschoff bodies, but in this case the proliferation was more diffuse than in the so-called foci or Aschoff bodies. In some places, especially in the crevices, hyaline masses of platelet thrombi were seen.

This is the typical picture of rheumatic valvulitis. It is essentially a proliferative process, in contradistinction to the valvulitis in bacterial endocarditis. At the time of autopsy one of the wartlike growths on the mitral valve was crushed and stained for bacteria. No organisms were found, although numerous large Aschoff cells were seen.

Progress in Pediatrics

RENAL RICKETS WITH METASTATIC CALCIFICATION AND PARATHYROID DYSFUNCTION

FRANCIS SCOTT SMYTH, M.D.
AND
LEON GOLDMAN, M.D.
SAN FRANCISCO

There have been many excellent reports on the demineralization of bone in association with chronic diffuse nephritis (renal rickets), but the condition is still imperfectly understood. To quote Hunter,[1] "the theory that phosphate retention, due to the renal defect, is primarily responsible for the changes in the bones is clearly unsatisfactory." The dwarfing, polyuria and polydipsia, which are not infrequent and which strongly suggest an endocrine factor, are likewise unexplained. A lemon yellow tint to the skin, anemia and weakness of the musculature are commonly associated with chronic nephritis, but these conditions are also found in hyperparathyroidism. The case summarized in the following report is of interest because of the opportunity it afforded to study some of the metabolic and pathologic factors in detail.

REPORT OF A CASE

History.—D. R., a boy aged 14 years, was referred to the pediatric service in April 1932 with the following history: He had a heritage better than the average and had had a normal birth and development. His childhood diseases, pertussis and measles, were without known complications. In February 1930 a streptococcic infection developed in a right finger; this was complicated by lymphangitis and an axillary abscess and was accompanied by a temperature of from 101 to 103 F. for two weeks. After the boy had been ambulatory for two weeks, during which time the abscess was draining, his temperature suddenly rose to 103 F., and a "scarlet fever" rash developed. Two weeks later a diagnosis of streptococcic septicemia was made, and, following that, a diagnosis of nephritis and secondary anemia.

A low protein, salt-free diet and tonics were used, but the patient continued to feel "all in," and his hemoglobin remained between 45 and 55 per cent.

Late in May 1931 he entered the hospital because of an attack of hay fever which cleared rapidly. He was dismissed on a diet of 40 Gm. of protein, 140 Gm. of fat and 145 Gm. of carbohydrate, making a total of 2,000 calories. In July 1931

From the Departments of Pediatrics and Pathology, University of California Medical School.

1. Hunter, D.: Critical Review: The Metabolism of Calcium and Phosphorus and the Parathyroids in Health and Disease, Quart. J. Med. **24**:393 (April) 1931.

he complained of pain in the right hip on walking; this was relieved by rest. The limp of the right foot, observed at this time, was thought to be caused by an irritation from his shoe. In October he complained of stiffness of the anterior portions of the thighs after being in one position any appreciable length of time, and a "waddling" gait developed.

By January 1932 he could not raise the right leg in climbing stairs and had a marked weakness in the muscles of the legs and pelvic girdle. He was seen by a neurologist, who made a diagnosis of progressive muscular dystrophy.

Examinations.—When admitted to the University of California Hospital on April 19, 1932, the patient had the general appearance of an emaciated, white male child with freckled skin of subicteric tinge. He was mentally alert and cooperative. His slumping posture and waddling gait resembled those seen in dislocation of the hip. His weight was 75½ pounds (34.23 Kg.); it had been 83 pounds (37.6 Kg.) in May 1931.

The following findings in the physical examination are worth noting: The skin had a velvety texture, and the mucous membranes were pale. The sandy-colored hair was thick and dry, though the eyebrows and eyelashes were thin. The pupils and perimetric fields were normal. The fundi showed indistinct margins of the disks but no cupping; there were no hemorrhages or exudates. There was no tenderness of the maxillary sinus. The teeth were in good condition and the tonsils had been removed. No rigidity of the neck was found, but flexion caused pain in the thoracolumbar region of the spine. There were prominent bilateral carotid pulsations. The thyroid was not palpably enlarged. The chest showed a marked increase in the anteroposterior diameter, a prominence of the sternal ends of the clavicles, particularly of the right, a bilateral accentuation of the infraclavicular fossae, and a flaring of the lower portion of the thoracic cage with beading at the costochondral junctures. The lungs were clear. Examination of the heart showed the apical impulse in the fifth interspace in the midclavicular line, a normal area of cardiac dulness, an accentuation of the pulmonic second sound and a soft blowing mitral systolic murmur. The radial arteries were compressed with difficulty. On entrance the blood pressure as determined on the right arm was 110 systolic and 56 diastolic; on the left arm it was 96 systolic and 56 diastolic; on the right leg, 112 systolic and 76 diastolic, and on the left leg, 108 systolic and 68 diastolic. The abdomen was flabby. The edge of the liver was just palpable at the costal margin. There was shortening of the phalanges. A scar was seen in the right axilla. The patient had a bilateral weakness of the deltoids and adductors of the thigh, and he held his feet in an equinovarus position. His reflexes were normal.

Subsequent Course.—After complete studies had been made and a transfusion given, the patient was discharged from the hospital on May 12. The laboratory observations on his first and subsequent admissions are shown in table 1. The alkaline-ash diet on which he was placed when going home was tolerated well for a week; then a persistent anorexia developed. In August he contracted a cold with fever followed by an irritative nonproductive cough which often caused vomiting. On August 21, when he reentered the hospital, he was hardly able to walk. Additional findings at this time were dyspnea, cough and a markedly dry skin. His framework had undergone marked changes, and the shoulder girdle was entirely relaxed and drawn forward. At the right coraco-acromial joint there was a malleable mass 4 cm. in diameter which seemed to be attached to the clavicle. At the sternoclavicular joints there were soft tumors; that on the right was the larger (fig. 1). There was no limitation of motion in the shoulder joints except that occasioned by weakness, and there was no pain on motion. The ribs

TABLE 1.—*Tests for Renal Function, Urinalyses and Examinations of the Blood on Successive Admissions*

Date	Urinalysis	Phenolsulphonphthalein Test	Mosenthal Test	Urea Clearance Test	Blood Chemistry		Blood	Blood Pressure
4/19/32 to 5/12/32	Albumin, faint trace; white blood cells, occasional; Esbach test, 0.5 to 1 Gm.	4/21: 1st hr., 2%; 2d hr., 5% Total: 7% 4/28: 1st hr., 1%; 2d hr., 2% Total: 3%	Day, 680 cc.; night, 150 cc. specific gravity, 1.005-1.008	9.7 cc. of blood per minute cleared; function, 18.1%	Albumin Globulin Nonprotein nitrogen Chlorides (whole blood) Carbon dioxide* Calcium Phosphorus	4.5 1.5 80.0 456.3 49.6 11.7 12.0	Hemoglobin, 55%; red blood cells, 2,860,000; white blood cells, 6,700; polymorphonuclears, 55%; 5/3. Hemoglobin, 35%; red blood cells, 2,460,000; white blood cells, 6,850; polymorphonuclears, 87%; lymphocytes, 10%; monocytes, 2%; eosinophils, 1%	Right arm, 110/56; left arm, 96/56; right leg, 127/76; left leg, 108/68
8/21/32 to 8/27/32	Albumin, heavy trace; white blood cells, 1-2 per high power field; red blood cells, occasionally	1st hr., 1%; 2d hr., 2% Total: 3%	Day, 520 cc.; night, 150 cc. specific gravity, 1.000 to 1.009	6.75 cc. of blood per minute cleared; function, 12.6%	Nonprotein nitrogen Chlorides Calcium Phosphorus	138.0 455.0 10.5 12.5	Hemoglobin, 30%; red blood cells, 1,860,000; white blood cells, 4,950; polymorphonuclears, 50%; polymorphonuclear basophils, 1%; stab forms, 6%; juvenile forms, 1%; lymphocytes, 33%; monocytes and transitionals, 8%	Right arm, 132/78; left arm, 96/56; right leg, 127/76; left leg, 144/85
9/20/32	.....	.....	.....	.....	Nonprotein nitrogen Calcium Phosphorus Phosphatase	142.0 10.9 10.9 10.7	Hemoglobin, 37%; red blood cells, 1,500,000; white blood cells, 4,760; polymorphonuclears, 83%; eosinophils, 1%; lymphocytes, 14%; transitionals, 2%	
10/20/32 to 11/3/32	Albumin, very heavy trace; white blood cells, clumps; casts, occasional, granular	.....	.....	1.9 cc. of blood per minute cleared; function, 3.4%	Nonprotein nitrogen Carbon dioxide Calcium Phosphorus Phosphatase 11/2 Nonprotein nitrogen Calcium Phosphorus	240.0 49.3 11.1 12.2 7.5 333.0 11.9 16.0	Hemoglobin, 30%; red blood cells, 1,570,000; white blood cells, 6,720; polymorphonuclears, 68%; small lymphocytes, 30%; immature monocytes, 2%; nucleated reds	

* The amount of carbon dioxide was calculated on the plasma content, not on the capacity.

appeared to have retracted from the sternum and its cartilage, so that the latter projected like a breast plate. The hands showed shortening of the metacarpals, phalanges and nail beds with ventral bowing of the phalanges and painless enlargement of the interphalangeal joints. The only painful enlargement was that of the left fifth distal interphalangeal joint. The nails were dry, brittle and marked with transverse ridges.

He was given a transfusion and an alkaline-ash diet and calcium gluconate. For the next three weeks he was bedridden because of weakness. He returned September 21 to receive a transfusion. The bony tumors had increased in size; his breath was urinous, and his respirations were rapid and shallow. The transfusion seemed to give him symptomatic relief, and he was taken home the same day.

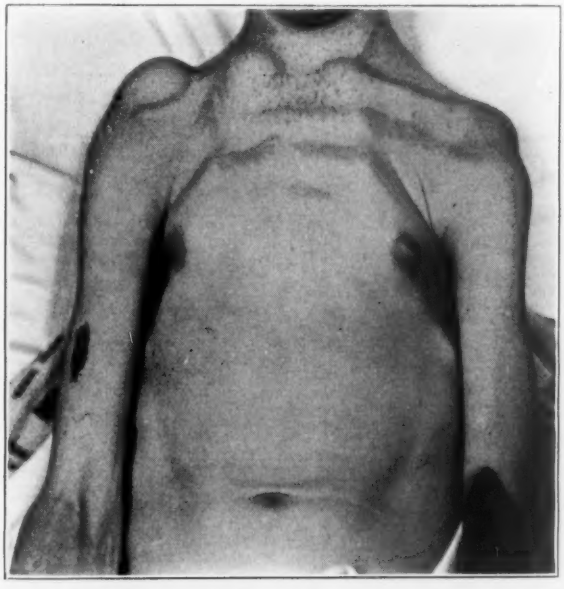

Fig. 1.—Photograph of the patient taken six weeks before death, showing masses at the clavicular and sternal junctures and acromial processes of the scapula.

On October 20 he returned in a miserable condition. He complained of stinging, burning pain in the lower extremities and of intense itching of the skin. The bulbous masses at the ends of the bones had increased in size (fig. 1), and the one at the costochondral juncture of the fourth rib on the right had become tender. There was a purple mottling of the extremities. The arteries had become prominent because of generalized wasting of the subcutaneous tissue, and on palpation they were almost rigid. He had frequent epistaxis, was weak to the point of helplessness, and was constantly nauseated. His diet, chiefly liquid, was retained poorly. On Nov. 3, 1932, generalized spasmdoic twitching of the muscles developed, and he died in a convulsion.

Roentgenographic Findings.—On April 20, 1932, roentgenograms of the right hand, wrist and ankle showed coarse trabeculations and rarefaction. The meta-

physes of the metacarpals showed irregular enlargement, and the lower ends of the diaphyses of the right tibia and fibula had a toothed appearance (fig. 2).

On May 2, 1932, the lungs showed considerable bronchial thickening, and at the base of the right lung there were two rounded masses in the pleura anteriorly which suggested a metastatic malignant degeneration (fig. 3). The outline of the epiphyseal ends of the long bones was ragged.

On Aug. 22, 1932, the cortex of the long bones was honeycombed, and the medullary canals appeared to be filled with cancellous bone. Many of the epiphyseal lines were becoming so disorganized that there appeared to be slight epiphyseal slippings. These changes were consistent with those of renal rickets.

Fig. 2.—Roentgenogram showing thinning of the bony structure and toothed diaphyseal changes in the tibias and fibulas.

On Aug. 24, 1932, there were tremendous overgrowths of irregularly calcified tissue at the ends of nearly all the ribs, at both ends of the right clavicle and on both acromial processes. These overgrowths arose in the positions where before there had been changes considered to be the result of rickets. The shadows of the fossae of both kidneys were very small. There was an overgrowth of the innominate bones at the acetabula. In the right hand, small calcified tumors were seen lateral and medial to the distal end of the proximal phalanx of the fifth digit and in the same position on the radial sides of the fourth, third and second digits. These tumors appeared to be joined to the bone by small pedicles. There were two larger tumors in similar positions in the left hand.

On Oct. 20, 1932, the roentgenograms of the skull showed a mottled appearance of all the cranial and of most of the facial bones and an increased thickness of the former. The falx cerebri and the tentorium were densely calcified (fig. 4). The nodular overgrowths were larger and more calcified than on previous examination (fig. 5).

The clinical diagnoses were: (1) chronic interstitial nephritis; (2) renal rickets with dwarfism; (3) metastatic calcification, and (4) possible dysfunction of the parathyroid glands.

The salient features of the case were: A boy, aged 14, dwarfed in stature and with a history of focal glomerular nephritis showed: (1) marked loss of muscle tone and power; (2) anemia with leukopenia and a lemon yellow tint to the skin;

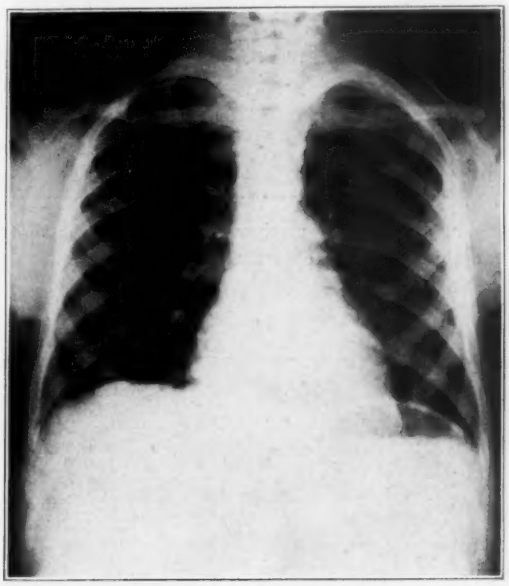

Fig. 3.—Early roentgenogram showing the first metastatic calcification at the costochondral juncture but suggesting pleural involvement at the base of the right lung.

(3) polyuria; (4) anorexia; (5) tenderness of the bones and early kyphosis; (6) some loss of hair, and (7) ridging of the nails.

Most of these findings have been listed with the clinical syndrome of hyperparathyroidism [2] in which osteitis fibrosa cystica is revealed by roentgenography. Some of the findings, the ectodermal lesions, for example, have been reported in association with hypofunction of the parathyroid glands.[3] Our study of this patient showed a marked impairment of renal function and generalized demineralization of bone comparable to the florid type of so-called renal rickets.

2. Bauer, W.: Hyperparathyroidism: A Distinct Disease Entity, J. Bone & Joint Surg. **15**:135 (Jan.) 1933.

3. Jacques, L.: Cataract and Postoperative Tetany, Am. J. M. Sc. **175**:185 (Feb.) 1928.

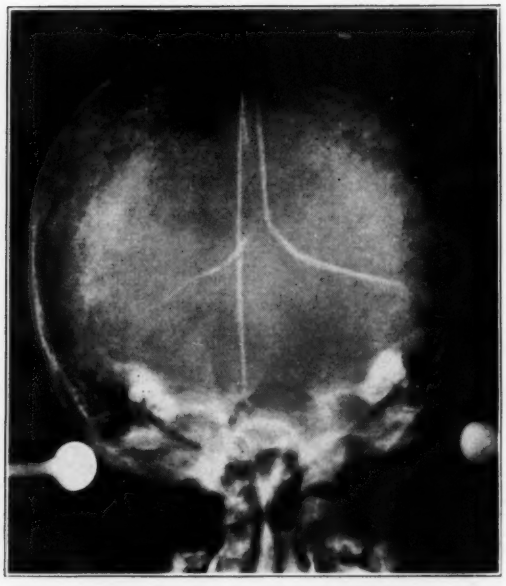

Fig. 4.—Roentgenogram of the cranium showing thinning of the cranial bones with so-called "woolly type" of appearance and calcification of the falx cerebri and tentorium cerebelli.

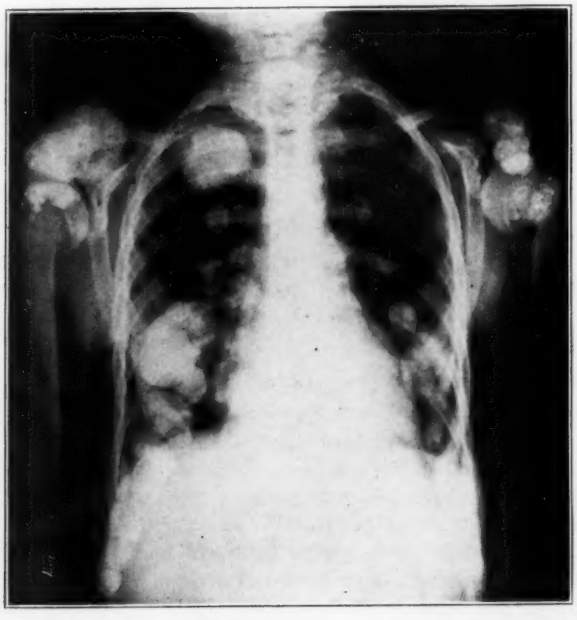

Fig. 5.—Roentgenogram of the chest showing immense areas of metastatic calcification at the costochondral junctures, acromial tumor masses and rarefaction of the humeri with slipping at the epiphyseal lines.

Studies were made on the metabolism of the calcium and phosphorus according to the method of the Medical Clinic of the Massachusetts General Hospital.[4] These studies showed a marked elevation of the level for calcium and phosphorus in the blood, an increased fecal excretion of calcium and a marked renal retention of phosphorus (table 2).

In comparison with other reports our observations show: (1) a negative balance for calcium on a low calcium intake. The negative balance is of the same magnitude as that for normal adults; (2) a positive balance for calcium on a high calcium intake, the retention in our case being twice as great as that reported by Sherman and Hawley;[5] (3) a slightly greater percentage of excretion of calcium in the stools as compared with that of normal adults; (4) a retention of phosphorus of far greater magnitude than has been shown by Sherman's figures for children on a high intake (the same in comparison with Abeloff's[6] study); (5) about the same percentage of excretory ratio of phosphorus between

TABLE 2.—*Calcium and Phosphorus Metabolism*

Diet	Stool	Urine	Total	Intake	Balance	Blood
Normal diet						
Calcium	0.213	0.071	0.284	.....	.....	12.2
Phosphorus	0.112	0.338	0.450	.....	.....	12.2
Low in calcium						
Calcium	0.165	0.055	0.220	0.106	−0.114	12.4
Phosphorus	0.087	0.263	0.350	0.892	+0.542	11.4
High in calcium						
Calcium	0.117	0.059	0.236	2.015	+1.779	10.9
Phosphorus	0.066	0.199	0.265	1.395	+1.130	12.0

stool and urine as in adults but a higher figure for urinary phosphorus than in Abeloff's case (a child with multiple cystic demineralization of the bone). In other words, our patient was not losing the minerals in abnormal amounts when he was depositing metastatic areas of calcification.

These findings are unlike those of reported cases of hyperparathyroidism in adults, in which there is more marked loss of calcium, chiefly in the urine, together with a hypercalcemia and hypophosphatemia. Obviously the severe renal dysfunction distorted the picture. It should be mentioned, however, that Wilder[7] reported a case of typical generalized osteitis in which there was no disturbance in the levels for

4. Bauer, W., and Aub, J. C.: Studies in Inorganic Salt Metabolism: I. Ward Routine and Methods, J. Am. Dietet. A. **3**:106 (Sept.) 1927.

5. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375 (Aug.) 1922.

6. Abeloff, A. J.; Sobel, I. P., and Bernhard, A.: Extensive Decalcification of the Bones in an Eight Year Old Boy, Am. J. Dis. Child. **45**:105 (Jan.) 1933.

7. Wilder, R. M.; Camp, J. D.; Robertson, H. E., and Adams, M.: A Fatal Case of Hyperparathyroidism with Report of Necropsy, Proc. Staff Meet., Mayo Clin. **7**:597 (Oct. 19) 1932.

calcium and phosphorus in the blood (there was, however, elevation of the phosphatase), but in which a definite adenoma of the parathyroid gland was found. Hence, it seems that the laboratory observations do not always conform to expectation, even in the absence of pathologic changes in the kidney.

Studies on magnesium and phosphatase were made. Recently magnesium has been considered of importance in relation to bone metabolism. In general it may be said to parallel the calcium metabolism but to show a variation far greater than the latter (200 per cent variation for magnesium and 30 per cent variation for calcium). Matthews and Austin [8] have shown that magnesium, as measured by the tone of the cardiac muscle, has an antagonistic relationship to parathyroid extract. They demonstrated that this mineral is less active in the presence of hypercalcemia than with the normal blood level and more active in the presence of hypocalcemia.

Jenner and Kay [9] showed an accelerating effect of magnesium on the hydrolytic and synthetic action of phosphatase. There is also some

TABLE 3.—*Magnesium Metabolism* *

Hematocrit	14.50	16.90
Magnesium, whole blood	5.40 mg. per 100 cc.	4.95 mg. per 100 cc.
Magnesium, plasma	4.68 mg. per 100 cc.	3.51 mg. per 100 cc.
Estimated corpuscular magnesium	9.66 mg. per 100 cc.	11.99 mg. per 100 cc.

* The normal values for serum were from 1 to 3 mg.; the cell values, from 2.5 to 4 per hundred cubic centimeters.

experimental evidence that magnesium inhibits calcification and, conversely, that diets low in magnesium produce decalcification in rats (table 3).

The phosphatase content of the serum has been found elevated in many pathologic changes of bone. The normal enzyme content, which is about 6 units or slightly higher in the blood serum of growing children, has been reported as being extremely high in osteitis fibrosa cystica (in the generalized but not in the focal type), in Paget's disease and in renal rickets. It might even be considered by some as an indication of parathyroid involvement. Our patient showed values ranging from 7 to 11 units, which is elevated, though not to the extent characteristic of similar extensive decalcifications. (The values of phosphatase found by Jenner and Kay for osteitis fibrosa cystica were as high as 170 units.)

8. Matthews, S. A., and Austin, W. C.: The Effect of the Blood Calcium Level on Tolerance to Magnesium; Hypercalcemia Induced by Parathyroid Hormone, Am. J. Physiol. **79**:708 (Feb.) 1927.

9. Jenner, H. D., and Kay, H. D.: Plasma Phosphatase: III. A Clinical Method for the Determination of Plasma Phosphatase, Brit. J. Exper. Path. **13**:22 (Feb.) 1932.

Under continued study, generalized calcification of the soft tissues was observed in connection with demineralization of the skeleton. At this time, because of the persistently lowered plasma bicarbonate and the clinical observation that the patient thrived better on an alkaline and calcium diet, he was given an alkaline-ash diet and calcium gluconate by mouth. Vitamin D and irradiation therapy were avoided as they are usually considered ineffectual, if not harmful, in renal rickets.

The patient died in uremic convulsions, though it is interesting to note that, despite an obvious sclerosis of the vessels, the blood pressure was not as high as might have been expected.[10]

AUTOPSY

The body was as described on entry except for cachexia (the weight was 55 pounds [24.9 Kg.]). The skin had a pale yellowish tinge. The teeth appeared in good condition. There were a few small shotty cervical lymph nodes. The thyroid gland was palpable. Soft masses were attached to the acromia, sternoclavicular articulations, spinous processes of the vertebrae, phalanges and metacarpal bones. The chest was pigeon-breasted with Harrison grooves and anterior and posterior rosaries of large globoid soft masses at the costochondral junctures. The abdomen was scaphoid. The fingers were short and stubby with a thick palmar and wrinkled dorsal skin like that of a laborer. Clubbing of the terminal phalanges and transverse ridging of the nails, lumbodorsal scoliosis and marked lumbar lordosis were present. There were purpuric spots and small ulcerations of the legs and arms.

The tumors of various size comprising the rosary and the soft masses attached to the bones proved to be of a yellowish, homogeneous, gritty, butter-like material both in a thick liquid as well as in a solid form, which on drying became chalklike. Chemical analyses showed the material to be calcium phosphate. A general examination of the abdominal cavity revealed no abnormalities except an enlarged liver which projected 8 cm. below the costal margin.

The thymus weighed 7 Gm.; it was white and unilobed. The pericardial sac contained 20 cc. of clear fluid. The heart was enlarged and weighed 225 Gm. The myocardium of the left ventricle was hypertrophied to 1.2 cm. in thickness, and on section revealed whitish-yellow deposits of calcium. A few mural atheromatous plaques were found near the leaflets. The valves and pericardium were normal.

The thoracic and abdominal portions of the aorta showed a few intimal atheromatous deposits. The iliac arteries were thickened and had hard calcareous deposits in their walls.

The kidneys were similar (each weighed 35 Gm.). They were shrunken by fibrosis and presented a bosselated surface. The pelvis and calices were markedly dilated, and the parenchyma was thinned (fig. 6). On section, the parenchyma showed an irregular pitted surface, a loss of cortical and medullary characteristics, and deposits of calcium. There was a marked hydro-ureter on each side and a hypertrophied trabeculated bladder. The urethra was not removed.

10. The blood pressure which often is not elevated in renal rickets is likewise not reported as being markedly elevated in most of the instances of hyperparathyroidism which we have reviewed. Hypothesizing from their experimental work, but without measurements, Matthews and Austin [8] expressed the opinion that the blood pressure is elevated in moderate hypercalcemia and lowered in hypocalcemia.

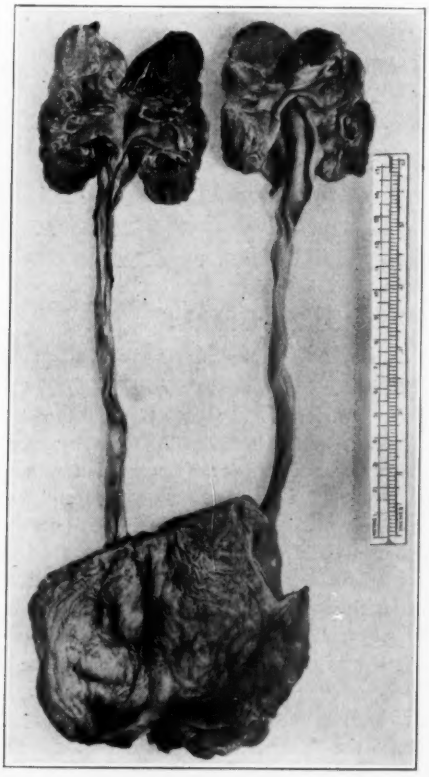

Fig. 6.—Bilateral hydronephrotic kidneys with metastatic calcification. Hydroureters and trabeculated hypertrophied bladder.

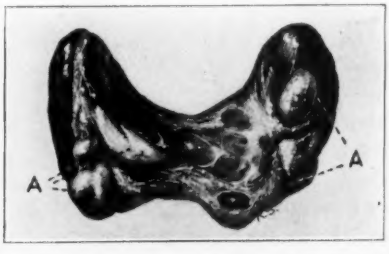

Fig. 7.—Drawing of the thyroid gland (posterior view) showing the five hyperplastic parathyroid bodies (*A*).

There were five yellowish-brown hypertrophied parathyroid bodies which varied in size from 0.5 by 0.4 by 0.3 cm. to 1.4 by 0.7 by 0.7 cm. (fig. 7). Section showed no lobulation or adenomatous formation, but merely a dense diffuse hyperplasia of the cellular constituents.

The skull was enlarged, thickened and square, with prominent bosses. The bones were soft; they could be indented on pressure and cut with a knife. The dura mater was thickened and calcified throughout, the process being more marked in the tentorium cerebelli. The brain was normal. The right middle ear and mastoid air cells were filled with thick green pus which yielded the colon bacillus and pneumococcus type IV on culture. The bone in this region was necrotic. The long bones revealed soft spongy trabeculae without evidence of any compact cortical bone. The medullary canal was filled with this spongy bone.[11]

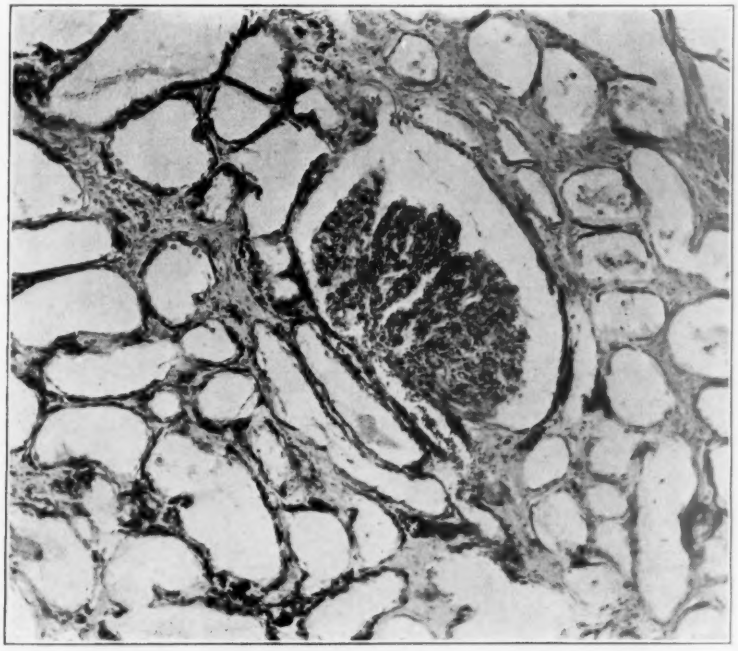

Fig. 8.—Section of a kidney showing hydronephrosis and metastatic calcification involving the convoluted tubules, Bowman's capsules and the arteries and arterioles.

The gastro-intestinal tract, lungs, liver, gallbladder, bile ducts, spleen, pancreas, suprarenals, external genitalia, seminal vesicles, testicles, thyroid, hypophysis and spinal cord showed no appreciable gross abnormalities.

Microscopic Examination of Important Sections.—In the heart there were calcareous granules and plaques in and between the muscle fibers, calcification of the coronary arteries involving the entire wall in some instances and only the internal elastic lamellae in others, and a diffuse patchy interstitial fibrosis. The endocardium and pericardium had no calcification and no other changes. The lungs were normal except for the presence of deposits of calcium attached to the alveolar walls and for calcareous changes in the arterioles. The smaller arteries

11. The chemical analysis showed: 20.92 mg. of calcium and 11.54 mg. of phosphorus per hundred milligrams of dry bone.

of the spleen showed calcification of the internal elastic layer. Calcium was found distributed in the walls of the mucosal glands, tunica propria and arteries and arterioles of the submucosa and muscularis of the fundus of the stomach, while sections from the pyloric region and remaining portion of the gastro-intestinal tract were free from calcification.

Metastatic calcification was found in Bowman's capsules and in the tubules, arteries and arterioles (fig. 8). The glomerular tufts were lobulated, contained hyaline deposits and presented adhesions to their capsules. Cross-sections of the dilated tubules revealed merely calcareous rings without epithelium. Interstitial fibrosis was marked, and many groups of chronic inflammatory cells were found throughout the sections, indicating a recent inflammatory reaction. The muscularis of the bladder was hypertrophied, and the small arteries were calcified. Small

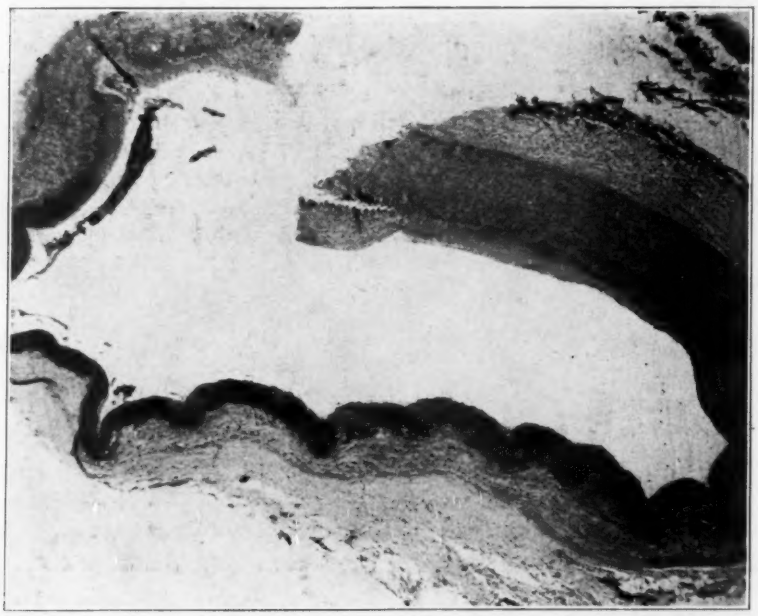

Fig. 9.—Section of the common iliac artery with calcification of the intima and fibrous tissue proliferation of the intimal and subintimal layers.

areas of fine granular deposits of calcium were found along the intima of the aorta. The external iliac arteries exhibited the most marked calcification of any of the vessels studied (fig. 9); it involved one-half the thickness of the vessel along its intimal border. Several aortic lymph nodes were enlarged and showed an endothelial hyperplasia. Calcification was also found in the walls of the small arteries of the pancreas. There was marked thymic involution with great enlargement and increase in the number of Hassall's corpuscles and a decreased amount of lymphoid tissue.

Microscopic sections of the parathyroids revealed dense, compact sheets of uniformly stained chief cells among which were a few groups of oxyphils (fig. 10). The morphology of the cells was not changed from the normal; there was merely a diffuse hyperplasia.

The suprarenal, thyroid and pituitary glands presented no unusual appearance on microscopic examination.

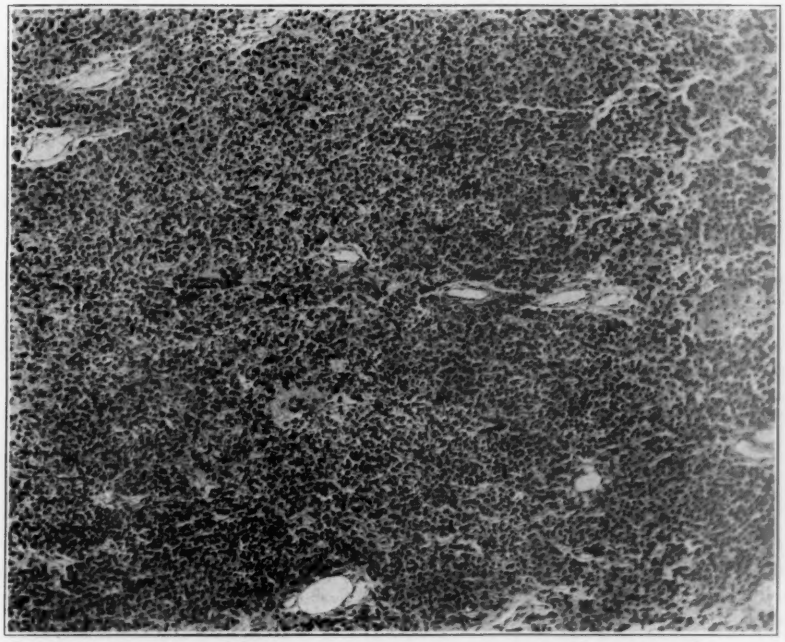

Fig. 10.—Parathyroid gland showing diffuse hyperplasia of its principal cell type.

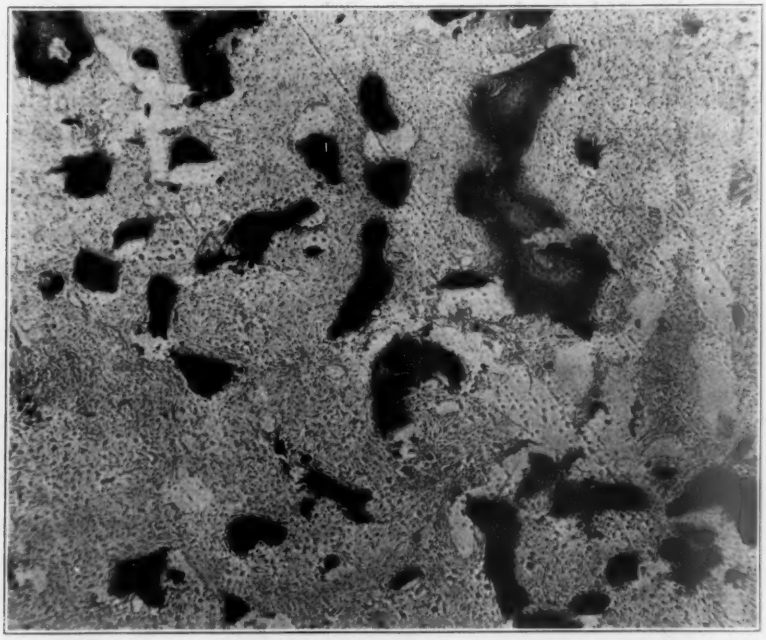

Fig. 11.—Section of bone showing decalcification, replacement by fibrous tissue and active lacunar osteoclastic activity.

Sections of the bones showed a replacement of the bony structures by a relatively cellular, old fibrous tissue (fig. 11). The lamellae were thinned, with ragged edges which showed lacunar resorption, and they varied in their calcium content. Osteoclastic predominated over osteoblastic activity. The microscopic picture was similar to that found in osteitis fibrosa cystica or Paget's disease. The epiphyseal lines were irregular and widened, and presented only slight evidence of active ossification. Sections of the bone marrow showed a hyperplasia of all the hematopoietic elements. The fibrous layers of the dura mater were heavily calcified, so that there were many bony spicules, several of which had well formed lacunae surrounded by osteoclasts.

The liver, gallbladder, prostate, testes and seminal vesicles, skin, skeletal muscle, brain and spinal cord showed no appreciable microscopic abnormalities.

The following pathologic-anatomic diagnosis was made: (1) bilateral hydronephrosis, hydro-ureter and hypertrophy of the urinary bladder; (2) demineralization (osteoporosis) of the bony skeleton with partial replacement by fibrous tissue; (3) hyperplasia of the parathyroid glands; (4) metastatic calcification of the heart, kidneys, lungs, dura, mucosa of the fundus of the stomach, arteries and arterioles; (5) osteoid depositions at the costochondral junctures, clavicles, metacarpals, phalanges and acromial and spinous processes; (6) cachexia; (7) acute suppurative otitis media and mastoiditis on the right side, the culture showing Bacillus coli and the pneumococcus type IV; (8) terminal septicemia, the culture of blood from the heart showing Streptococcus viridans and Staphylococcus aureus; (9) hypertrophy of the left ventricle, and (10) accidental involution of the thymus gland.

COMMENT

Rôle of the Renal Lesion.—The hydronephrotic element, found at autopsy, is significant because developmental defects of this type are more than casual accompaniments of chronic diffuse nephritis.

Dwarfing, or infantile stature, is described with renal lesions of this type, and skeletal decalcification (renal rickets) is found in about 30 per cent of the cases. The dwarfing has not been explained. However, the present study, in which the parathyroids were obviously involved, suggests that Thompson's [12] antigrowth factor of the parathyroid may be of more than academic interest. The demineralization of the skeleton is commonly explained by the retention of, or the failure of the kidney to excrete, acid phosphate. A lowering of the plasma bicarbonate and serum calcium can then be expected. It should be mentioned, however, that cases of renal rickets have been reported in which there was no elevation of the phosphorus, and Hunter [13] said that "the theory that phosphate retention (due to renal defect) is primarily responsible for the changes in bones, is clearly unsatisfactory." Experimental evidence, on the other hand, supports the accepted theory, and the clinical studies

12. Thompson, J. H.: An Anti-Growth Factor (A Preliminary Communication), J. Physiol. **70**:xli (Oct.) 1930.

13. Hunter,[1] p. 433.

of Boyd, Courtney and MacLachlan [14] and of Schoenthal [15] give similar support. In our patient, study of the excretion showed chiefly a marked retention of phosphorus and only a slightly negative balance of calcium. The excretion of calcium, however, was preponderantly by way of the bowel; in fact, it was greater than that expected in normal adults.

It is of interest that Collip [16] has been able to simulate experimentally the effect of an overdosage of parathyroid extract-Collip by the injection of acid phosphate and calcium chloride.

Possible Secondary Parathyroidism.—Our present concepts regarding the pathologic changes in the parathyroid bodies are rather confused. The spectacular success of Mandl's [17] parathyroidectomy for osteitis fibrosa cystica has perhaps overshadowed the consideration of parathyroid dysfunction of a secondary nature. A fairly large group of clinicians accept the relationship between the hyperfunction of the parathyroid gland and demineralization of the bone as simply one of cause and effect. A more conservative group restricts the syndrome of hyperparathyroidism to the disease entity of adenoma of one parathyroid gland and cystic changes in the bone. The adolescent focal type of osteitis fibrosa cystica, as described by Hunter,[18] lacks these characteristics and hence would not be benefited by parathyroidectomy.

Unfortunately, routine examination with microscopic sections of the parathyroids has been overlooked by most pathologists. Certain pathologic studies strongly suggest the probability of parathyroid involvement of a secondary type. Erdheim [19] found evidence of parathyroid hyperplasia and hypertrophy in experimental rickets of rats and in some instances of infantile rickets. Bauer [20] and others reported the same observations in clinical cases of osteomalacia. The parathyroid enlargement in hematogenous myelomatosis, reported by Bulger,[21] and in carcinomatosis of the bone also suggests secondary involvement rather

14. Boyd, G. L.; Courtney, A. M., and MacLachlan, I. F.: The Metabolism of Salts in Nephritis: 1. Calcium and Phosphorus, Am. J. Dis. Child. **32**:29 (July) 1926.

15. Schoenthal, L., and Burpee, C.: Renal Rickets, Am. J. Dis. Child. **39**:517 (March) 1930.

16. Collip, J. B.: The Production of Some of the Phenomena Peculiar to Parathyroid Overdosage in Dogs by Means of Certain Inorganic Salts, Am. J. Physiol. **76**:472 (April) 1926.

17. Mandl, F.: Klinisches und Experimentelles zur Frage der lokalisierten und generalisierten Ostitis fibrosa, Arch. f. klin. Chir. **143**:1, 1926.

18. Hunter,[1] p. 415.

19. Erdheim, J.: Rachitis und Epithelkörperchen, Denkschr. d. Akad. d. Wissensch. Math.-naturw. Klasse, Wien. **90**:363, 1914.

20. Bauer, T.: Ueber das Verhalten der Epithelkörperchen bei der Osteomalacie, Frankfurt. Ztschr. f. Path. **7**:231, 1909-1910.

21. Bulger, H. A.; Dixon, H. H.; Schregardus, O., and Barr, D. P.: Functional Pathology of Hyperparathyroidism, J. Clin. Investigation **9**:143 (Aug.) 1930.

than a primary cause. The question has been discussed by Albright and his coworkers,[22] who advanced the hypothesis that hyperparathyroidism may exist as a secondary phenomenon in the group of disorders in which the calcium and phosphorus of the blood are so reduced as to represent "subsaturation." He suggests that a low level for blood calcium is the stimulus for the secretion of the parathyroid gland. While the study of our patient at no time showed subsaturation but, on the contrary, an elevation of the levels for both calcium and phosphorus, it is possible that such a state existed before our observations were made.

Before accepting this hypothesis of secondary hyperparathyroidism, we suggest that an elevated blood phosphorus may as likely be a trigger phenomenon as lowered calcium. In osteomalacia, certain types of experimental rickets and tetany, all of which have been described with associated parathyroid hyperplasia, elevation of the level for phosphorus may be as characteristic as the lowering of that for calcium. Aub and his co-workers [23] showed that the earliest effect of parathyroid hormone is on the phosphorus, which, by lowering the renal threshold, falls before an increase in calcium may be detected. This has been verified by other observers, though Thomson and Collip [24] do not find it compatible with some of their experiences.

In hyperparathyroidism there is a lowered threshold for the renal excretion of phosphorus. Reasoning by analogy is obviously open to criticism, but, with regard to our patient, it suggests that an elevation of the level for phosphorus may call forth parathyroid activity just as hyperglycemia apparently is the stimulus for insulin activity in the normal pancreas. A review of reported pathologic studies of renal rickets reveals little or no comment regarding parathyroid hyperplasia (i. e., microscopic as well as gross evidence of hypertrophy). Until further data are obtained, it is difficult to settle their possible relationship.

However, regardless of the sequence of events responsible, it is obvious that, in the presence of chronic renal impairment, parathyroid stimulation, as an attempt to adjust the mineral balance, establishes a vicious circle. The primary effect (described by Albright [22]) of the hormone acting on the renal threshold for phosphorus is defeated by the diminished function of the kidney, and supersaturation results.

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22. Albright, F.; Bauer, W.; Claflin, D., and Cockrill, J. R.: Studies in Parathyroid Physiology: III. The Effect of Phosphate Ingestion in Clinical Hyperparathyroidism, J. Clin. Investigation **11**:411 (March) 1932.

23. Albright, F.; Bauer, W.; Ropes, M., and Aub, J. C.: Studies of Calcium and Phosphorus Metabolism: IV. The Effect of the Parathyroid Hormone, J. Clin. Investigation **7**:139 (April) 1929.

24. Thomson, D. L., and Collip, J. B.: The Parathyroid Glands, Physiol. Rev. **12**:309 (July) 1932.

Hypercalcification.—The metastatic calcification is perhaps the most interesting feature of the case, yet perhaps there is little conjecture regarding its origin in our patient, since experimental studies have given considerable information on this aspect of the case.

Alkalinity has been incriminated in hypercalcification, not only by studies in lead poisoning but also by Hueper's [25] studies on metastatic calcification which demonstrated that calcification strikes the tissues in which acid is given off, with the result that the cells are locally more alkaline than the blood (i. e., stomach, lung, heart and kidneys). Calcification of the arteries and dura, however, is not explained by this phenomenon. In our patient an alkaline diet and calcium were prescribed after metastatic calcification had been observed, and the patient tolerated this diet (in the presence of chronic acidosis) better than an acid diet or one that was low in calcium. In further defense we shall cite two cases (discussed later) similar to ours except that there had been no dietary restrictions. In his recent review of calcinosis Barr [26] suggests that, in the presence of viosterol, a diet high in calcium plus acid gives rise to metastatic calcification.

Supersaturation of the blood with calcium and phosphorus appears to be an important factor. The experiments of Smith and Elvove [27] especially incriminate the phosphorus. Shelling [28] showed that diets minimal in calcium but high in phosphorus made his animals more susceptible to viosterol and the related calcification of soft tissues. Even in parathyroidectomized dogs increased retention of phosphorus characterized the metastatic calcification obtained in those experiments.

Hypercalcification has been produced experimentally by an excessive administration of vitamin D or parathyroid extract-Collip. Some investigators believe that the effects of these two substances given in excess are almost identical and that summation or aggravation results from the presence of both the hormone and the vitamin, while absolute restriction of the vitamin diminishes the effect of the hormone. Shelling, however, has shown that the effect of viosterol varies with the intake of calcium and phosphorus, and that an increased intake of phosphorus favors hypercalcification with viosterol. On considering either view, the avoidance of vitamin D in our clinical treatment of the patient was rational.

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25. Hueper, W.: Metastatic Calcifications in the Organs of the Dog After Injections of Parathyroid Extract, Arch. Path. **3**:14 (Jan.) 1927.

26. Barr, D. P.: Pathological Calcification, Physiol. Rev. **12**:593 (Oct.) 1932.

27. Smith, M. I., and Elvove, E.: The Action of Irradiated Ergosterol in the Rabbit, Pub. Health Rep. **44**:1245 (May 24) 1929.

28. Shelling, D. H.: Effect of Calcium and Phosphorus of Diet on Tetany and Serum Calcium of Parathyroidectomized Rats, Proc. Soc. Exper. Biol. & Med. **28**:301 (Dec.) 1930.

While recent discussions of metastatic calcification have called attention to its presence in some of the clinical cases of hyperparathyroidism and to its production by overdosage of parathyroid extract or vitamin D, the sequence of events in its production is often overlooked. From experiments it appears that early in the administration of parathyroid there is demineralization, a fall in serum phosphorus caused by renal excretion and a compensatory rise in calcium. (With vitamin D, the change in values for these elements in the serum is less noticeable.) In the toxic stage, however, metastatic calcification occurs in addition to decalcification of the structure of normal bone, and the serum phosphorus is elevated. At the same time there is a definite rise in nonprotein nitrogen and evidence of renal damage. We venture to suggest that renal injury is thus the first pathologic change to be demonstrated and is perhaps a large factor in the subsequent calcinosis elsewhere in the body. Recent experimental work [29] on calcification shows that degeneration of the cells of the kidney is the most constant early change observed and that it probably precedes the deposition of calcium. It seems to us that this observation is of peculiar significance not only with regard to the whole matter of calcinosis but also with regard to sclerosis of the arteries and kidneys with less generalized calcinosis, such as is seen in the reported cases of chronic diffuse nephritis.

Many of the reports of metastatic calcification have the factor of severe nephritis in common. Marsden's [30] case, that of an infant with renal disease and septicemia, might suggest sepsis as a factor. We should make the statement that in our patient the mastoiditis was a terminal part of the clinical course and hence definitely played no rôle in the production of aberrant calcification. Virchow [31] considered renal damage a necessary factor in calcinosis. It appears, then, that oversecretion of the parathyroid, hypercalcification and certain types of renal failure (chronic diffuse nephritis) are intimately related. Although the parathyroid condition is usually emphasized, we believe that in our patient the renal condition was primary.

Relatively few cases similar to this one have been reported. In 1901, Bryant and White [32] reported a case of calcifying endarteritis

29. Reed, C. I.; Dillman, L. M.; Thacker, E. A., and Klein, R. I.: Calcification of the Tissues by Excessive Doses of Irradiated Ergosterol, J. Nutrition **6:** 371 (July) 1933.

30. Marsden, J. P.: Metastatic Calcification: Notes on Twins Born Shortly After an Attack of Smallpox in the Mother, Brit. J. Child. Dis. **27:**193 (July-Sept.) 1930.

31. Virchow, R.: Kalkmetastasen, Virchows Arch. f. path. Anat. **8:**103, 1855.

32. Bryant, J. H., and White, W. H.: A Case of Calcification of the Arteries and Obliterative Endarteritis, Associated with Hydronephrosis in a Child of Six Months, Guy's Hosp. Rep. **55:**17, 1901.

obliterans and calcification in the endocardium, associated with great dilatation of the urinary tract in an infant 7 months of age. No mention was made of pathologic changes in the parathyroid gland. In 1905, MacCallum [33] gave a report on the pathologic changes found in a patient with chronic nephritis, but there were no reports on determinations of the blood chemistry, the condition of the bone or metastatic calcification.

In 1921, Hubbard and Wentworth [34] reported a case of chronic nephritis with an osteitis fibrosa involving the skull, ribs and vertebrae and with metastatic calcification and cystic masses similar to those described for our patient. In addition, two large hyperplastic parathyroids were found. The metabolic studies of these authors were limited, but the blood calcium varied from 13.4 mg. per hundred cubic centimeters on a high, to 11.9 mg. on a low, intake of calcium.

In the recent literature we have found only two reports of cases which resemble ours. Cooley,[35] in closing the discussion of his presentation at the 1931 meeting of the American Pediatric Society, mentioned having seen "an autopsy in a case of renal rickets in which hyperplasia of the adrenal cortex and the parathyroids and a remarkable eosinophilia of the pituitary body were found." Through correspondence he gave us more details and sent sectioned material for comparison.[36]

The second, somewhat similar case was reported by Lightwood [37] as a case of "Dwarfism and Calcinosis" in a child 2 years of age. The

33. MacCallum, W. G.: Tumor of the Parathyroid Gland, Bull. Johns Hopkins Hosp. **16**:87 (March) 1905.

34. Hubbard, R. S., and Wentworth, J. A.: A Case of Metastatic Calcification Associated with Chronic Nephritis and Hyperplasia of the Parathyroids, Proc. Soc. Exper. Biol. & Med. **18**:307 (May 20) 1921.

35. Cooley, T. B.: Hyperparathyroidism and Similar Diseases of the Bone, Tr. Am. Pediat. Soc. **43**:20, 1931.

36. In the case observed by Cooley, eosinophilia in the pituitary body and suprarenal cortical hyperplasia were described. No similar pathologic changes were found in these tissues of our patient. However, besides the possible rôle of an antigrowth element in the parathyroid, the dwarfing logically may depend on some secondary pituitary involvement. This pituitary involvement is suggestive of Cushing's observations on basophilic adenoma of the pituitary, in association with which there has occasionally been described a "peculiar softening of the bone." (Cushing, H.: Further Notes on Pituitary Basophilism, J. A. M. A. **99**:281 [July 23] 1932.) One such patient was studied by Aub (quoted by Cushing, p. 283), who found normal levels for the calcium and phosphorus but abnormal loss of calcium in the urine. Aub's conclusion was that the patient had a mildly overactive parathyroid. Some of the patients with Cushing's syndrome had suprarenal involvement which again suggests the pluriglandular changes reported by Cooley.

37. Lightwood, R.: Case of Dwarfism and Calcinosis Associated with Widespread Arterial Degeneration, Arch. Dis. Child. **7**:193 (Aug.) 1932.

calcium was 11 mg., and the phosphorus, 6.8 mg., per hundred cubic centimeters of blood in the one estimation reported. Though marked renal impairment was present, Lightwood did not consider the case one of renal dwarfism. The bones showed the characteristic alternating porosis and repair, but the calcification was not as extensive as in our patient. (Lightwood also sent us slides showing chronic glomerular nephritis and calcification of the myocardium, pericardium and arterioles.) The endocrine study in this case seems too brief to permit drawing conclusions. No tumor of the parathyroid gland was found, and only one gland, described as normal, was removed. We believe that this case represented an earlier phase of the same general condition in which the renal injury was primary.

We should like to emphasize the following interesting points: 1. Parathyroidectomy was mentioned but would have been futile in this type of condition.

2. Ingestion of phosphate, such as Aub [23] has suggested, would have been equally futile and, in the presence of the renal lesion, would have hastened death.

3. The teeth of our patient were exceptionally sound. This is of interest in view of the present tendency to draw close parallels regarding the formation of bones and of teeth.

SUMMARY

1. The case reported presents renal rickets, parathyroid dysfunction and metastatic calcification with complete clinical, laboratory and pathologic studies.[38] The rôle of each major organ in the disease complex is discussed.

2. The underlying pathologic condition was probably a congenital partial urethral obstruction with hydronephrosis. On this was superimposed a streptococcic infection which was manifested by clinical signs of severe diffuse nephritis.

3. The retention of acid phosphate constituted the first important change in the chemical constituents of the blood.

4. It is suggested that stimulation of the parathyroid glands by the high level of phosphorus in the blood (parathyroid hyperplasia) results in dwarfing and demineralization of the bones.

5. The supersaturation of the blood with calcium and phosphorus was followed by extensive and rapid calcification.

38. Langmead, F. S., and Orr, J. W.: Renal Rickets Associated with Parathyroid Hyperplasia, Arch. Dis. Childhood **8**:265 (Aug.) 1933. This article appeared after our presentation at the 1933 meeting of the American Pediatric Society and offers further corroboration for the condition we have reported.

TREATMENT OF WHOOPING COUGH

A STUDY IN THE HISTORY OF THERAPEUTICS

ISAAC A. ABT, M.D.
CHICAGO

The disease known as whooping cough has been described under a multiplicity of names. Willis (1622-1675) named it "tussis convulsiva," while Sydenham (1624-1689) called it "pertussis," which means a violent cough of any kind. There are other Latin names, the most striking among them being "quinta," "paroxysmes quintes" and "quintana." It is possible that these came to be used because the cough was observed to return every five hours. Other countries have their own descriptive terms. Besides the familiar name "whooping cough" we have in English "hooping cough," "kick cough," "kink cough," or simply "the kink," and the frequently used expression "chin cough." In Austria the disease is spoken of colloquially as *"Stickhusten"* (stick cough) or *"Krampfhusten"* (cramp cough). In Bavaria pertussis is called *"Blauhusten"* (blue cough).

Whooping cough cannot be definitely traced back further than the middle of the sixteenth century. It seems certain that Galen knew nothing of whooping cough, nor did the Byzantines, Romans or Arabs. The epidemics of coughing in the middle ages were probably not whooping cough. Elyot in his "Castel of Health" (1541) and Phaer in his "Boke of Children" (1553) did not mention the disease. The first authentic description was probably that of Baillou (Ballonius) in 1578. Nearly a century then passed before the treatises of Thomas Willis (1674) and Ettmuller (1685) were added to the literature of whooping cough. Sydenham mentioned it twice, once in his account of the epidemic of measles of 1670 and again when he included the "convulsive cough of childhood" in describing the epidemic of influenza of 1679. In Walter Harris' famous book, "Diseases of Children," (1689) the convulsive or suffocative coughs are mentioned in one place without being identified as chin cough, while in two or three other places the malady is briefly referred to. The physicians of that day seem to have considered whooping cough an affair for grandmothers, empirics and gypsies, and it was probably of more common occurrence than one would be led to believe from references in the literature. In the early

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President's address, Institute of Medicine, Chicago, Dec. 5, 1933.

part of the eighteenth century the names of Alberti (1728), Friedrich Hoffmann (1732) and John Burton (1738) were added to the list of authorities on this disease.

It is probable that whooping cough originated in large cities such as Paris and London and spread thence in all directions. The epidemic in France described by Baillou may be considered the first of its kind. The second epidemic appeared in London in 1658, but according to all accounts whooping cough had been endemic in London before that time. Since the middle of the seventeenth century numerous epidemics of whooping cough have been described. In 1695 many children died of it in Paris and in Rome. During a widespread epidemic in the middle of the eighteenth century the disease was carried to America. It did not occur in Australia until the middle of the nineteenth century, when it was introduced by European travelers. In Central America, Africa and Asia, this particular disease is said to be comparatively rare. Yet whooping cough is now fairly universal; it appears in either endemic or epidemic form and may affect any race in any climate.

All writers agree that the earlier epidemics were more severe than those of the present day. In Germany in the years 1815 and 1816 the death toll from whooping cough was particularly heavy. In England the mortality from whooping cough has been high at times; in the years from 1838 to 1853 3.4 and in 1877 2 per cent of all the deaths in London were due to whooping cough. In the United States reports covering a period of thirty years in the twentieth century show an average rate of mortality from whooping cough of 9.92 per hundred thousand of population. There is a slight decrease in the rate in successive decades. In the year 1932 300,000 cases were reported in the United States. The annual number of deaths from this disease in the United States is 6,000 or more. The younger the children the higher is the rate of mortality. One half of the deaths from whooping cough occur in infants under 3 months, and the high mortality persists in children under 3 years. Whooping cough, like measles, may activate latent tuberculous infection, death ensuing from the latter. Respiratory and nervous complications are numerous and are sometimes the immediate cause of death.

Weather, climate and seasonal conditions have always been thought to bear some relation to the incidence and virulence of epidemic diseases. Baillou described the summer of 1578 as being glowing and burning hot. Infants under 1 year were attacked by fevers and carried off in large numbers. Particularly prevalent was the variety of cough which was called "quinta." He described the symptoms of this disease, giving the first clearly recognizable account of whooping cough. The lung is so irritated that the infant can neither admit breath nor easily give it forth again. The sick person seems to swell up and holds his breath, as if

about to strangle. Further on, Baillou observed that the patient may be free from coughing for a space of four or five hours, the paroxysm then returning. It is sometimes so annoying that blood gushes out through the nostrils and mouth by violence. He added: "I have not yet read any author who writes about this cough."

Thomas Willis, in 1674, made some original observations regarding puerorum tussis convulsiva, or chin cough. He noted that the disease attacks principally infants and children and occurs most commonly in the spring and autumn. It is an epidemic disease characterized by paroxysmal coughing; the respiratory organs are subject to spasm, or they may be more gravely affected. Willis noted that the patients appear to be suffocating and become black in the face, and that their strength becomes exhausted.

Since the first recognition of whooping cough methods of combating it have been numerous and diverse. In all periods treatment of disease has depended on the enlightenment of the period and on the developmental stages of medicine. In reviewing the past history of medicine one is impressed by the influence of contemporary mysticism, natural philosophy and astrologic and alchemistic views, not to speak of superstition and belief in magic. The treatment of whooping cough has gone and, one may say, is still going through all the stages. In tracing the various methods of treatment applied to this disease changes in the practice of the healing art are seen to take place from the sixteenth century to the present time.

It has already been noted that many of the patients with whooping cough were left to the management of old women and gypsies; hence one is not surprised to learn that folk remedies of every kind have been employed and still persist in primitive communities. In Styria the disease was treated by evergreen berries from the woods and by sauerkraut used internally and externally. In the vicinity of Graz the common people collect the water which a horse has dropped while drinking and administer it to the baby with whooping cough. Before the patient has a meal the house dog must be given a bite to eat so as to drive away the child's cough. In Bavaria pertussis was treated by administering powdered lady-fly with potash. An odd custom in the same district consisted of tying up three large pieces of sugar candy in a pig's bladder, suspending it for twenty-four hours in flowing water and then giving the sugar solution to the patient, the pig's bladder meanwhile being thrown into the water. In Swabia cockroaches are fed to the children. In Constantinople sparrow's blood and sulphur wine are given. In Turkey women threw leaves of laurel or branches of pine in front of the patient in the form of a cross, set them on fire and let the patient inhale the smoke. Amulets have been used extensively, and in Malabar a bone of a crocodile was suspended about the neck of the patient.

It is the custom of a certain Indian tribe to have a child with whooping cough suck a feather taken from the wing of a crow. He is expected to hold this in his mouth until relieved, and if no relief is obtained by this means he must watch the road for a rider in gray apparel on a gray horse, who may be able to tell how the "gray cough" can be cured.

An ancient belief referred to in the writings of Pliny is that disease may be transferred to animals. Thus it was an old custom in Devonshire to practice transference by taking a hair from the head of a child with whooping cough, putting it between slices of bread and butter, and feeding these to a dog. If the dog coughed, as he usually did, the disease was transferred.

Even the taboo has its place in whooping cough therapy. When there was a case of whooping cough among the Mojave Indians of Arizona the head of the family was forbidden to touch coffee or salt while his child's illness lasted.

It was early recognized that whooping cough was infectious and that it occurred in epidemic form. J. Peter Frank (1745-1821), who wrote an important treatise on therapeutics and whose great work on public hygiene covered nearly the whole field of preventive medicine, said that the only prophylaxis consists in avoiding contagion. He also urged that precautions be taken against infection from clothes and household articles. Preventive drugs of various kinds have been suggested from time to time. Hahnemann (1755-1843) believed that the disease could be prevented by the use of tincture of wormwood. Others recommended belladonna. The use of salicylic acid was reported on favorably from Italy. But Jahn's (1805) words had a restraining effect on attempts at prophylaxis by medication. He said: "No dietetic treatment, no cleansing or strengthening by internal or external means, no amulet, has the power to protect against whooping cough if one cannot avoid the epidemic influences or infection." Even though no drug which has been tried up to the present time has proved to be a sure protective agent, the hope of finding some prophylactic remedy has never been abandoned.

During all recorded time there has been an instinctive striving to find some effective remedy properly prepared to combat human ailments. Vegetable remedies have been in use since the earliest times for the relief of illness, both by peasant folk and by professional healers. In the sixteenth century physicians again turned their attention to the study of plants and made botanical investigations for the advancement of the art of medicine. Botanically minded doctors collected herbs and wrote treatises about them. Important botanical gardens for growing medicinal plants were started in Italy, Germany, France and the Netherlands. The establishment of trade routes to America and India added the flora of these continents to the materia medica of the old world. Spanish physi-

cians were particularly active in importing drugs from the new world, and gradually their publications regarding them were translated into Latin and thus became the property of the practitioners of all Europe. It is to these developments in the pharmaceutic art that one owes the use of an amazing variety of vegetable substances in whooping cough: hemlock, pennyroyal, henbane, calisaya bark, tobacco, coffee, thyme, cyprus, guaiac and ipecac, to mention only a few.

Paracelsus (1493-1541), the great reformer in pharmaceutics and therapeutics, was the first to extract effective substances from such vegetable products by the use of alcohol as well as by distillation and sublimation.

The use of metals in the treatment of disease also dates from the time of Paracelsus. He introduced mercury, lead, iron, copper sulphate, potassium and sulphur and preparations of antimony, all of which have been used in one form or another for whooping cough. The development of the medical chemistry originated by Paracelsus was fostered in the next century by such men as van Helmont and de la Boë (Sylvius), who rendered the use of chemical medication more scientific through their chemical studies of the normal and pathologic functions of the human body. The growth of chemical knowledge in general is reflected in the additions of chemical substances to the list of agents regarded as remedies for whooping cough. One finds in that list ammonium salts, prussic acid, potassium, sulphur, arsenic and countless others.

Animal substances have been in use as healing agents for as long a time as vegetable substances. When the pharmacopeia underwent revision in 1745, many of the early animal products were retained. Mention has already been made of the use by primitive peoples of cockroaches and sparrows' blood. Toward the close of the eighteenth century one finds mentioned among remedies for whooping cough millepeds, calves' feet and cantharides.

The chronicle of early remedies for whooping cough would not be complete without mention of Christian Franz Paullini (1643-1712) of Eisenach, wandering physician, poet and historian, who was best known by his "Heilsame Dreckapoteka" (literally "healing dirt pharmacy"). This work is of considerable importance for the knowledge of popular medicine and folkways. It was stated that the quintessence of all food was contained in feces; hence it was only logical to suppose that that substance had healing properties. Dung of screech owls was prescribed for melancholy and dog dung and fleas boiled in sage for gout; hence one need not be surprised to learn that children with whooping cough were fed sweet milk boiled with the excreta from an ass. O therapy, what vagaries have been committed in thy name! Yet though one may shudder at earlier usages, one must not forget that only recently a significant hormone has been isolated from the urine of pregnant women.

The therapeutics of the eighteenth century was influenced by the chemical investigations of Stahl, Cavendish and Priestley and the physiologic studies of von Haller. There were added to the materia medica for whooping cough such substances as frangula, iceland moss, couchgrass root and other vegetables. The eighteenth century also saw an extension in the use of metallic preparations; gold sulphate, calcium and other metals came to be included among remedies for whooping cough. From Vienna during this period came recommendations for aconite, conium, hyoscyamus and pulsatilla, most of which were promptly tried on whooping cough.

The newer chemistry and physiology of the nineteenth century and general advances in scientific thought turned the minds of physicians and pharmacologists to the more scientific investigation of drugs. Animal experimentation and chemical investigation of medicinal substances were the natural sequence of the newer thought. The first pharmacologic institute was founded at Dorpat; special pharmacologic journals were established, and laboratories were started in many of the great universities during this period. The extensive studies on opium and its alkaloids carried on in France and other European countries are of importance from the point of view of whooping cough therapy. The introduction of iodine and iodine preparations is also noteworthy, and so too is the discovery of the use of ether, chloroform and chloral hydrate. Toward the close of the century organic chemical substances began to be used: acetanilid, acetphenetidin and phenol; the latter substance derived renown from its use by the great English surgeon, Lister. The antiseptics were received by the clinicians who were treating whooping cough with high hopes that they would be effective in destroying the bacteria which in those days already were thought to be the cause of the disease.

It was during this period that Rudolph Buchheim (1820-1879) of Dorpat published his textbook on materia medica. He also investigated the action of potassium salts, purgatives, cod liver oil, ergot and mydriatic alkaloids. The experimental work of Buchheim's pupil, Oswald Schmiedeberg, on digitalis and other drugs was published in his well known treatise, "The Elements of Pharmacology." Karl Binz (1832-1912) investigated the action of quinine, alcohol, arsenic and ethereal oils and the halogen compounds. Sir Thomas Lauder Brunton (1844-1916) correlated the physiologic findings of pharmacology with internal medicine.

One of the important therapeutic developments of the nineteenth century was the introduction of substances from internal organs as medicaments against disease. To this innovation may be traced the use of substances obtained from suprarenal glands advocated from time to time for whooping cough.

The treatment of whooping cough during successive periods depended largely on the physician's point of view and on his concept of the disease. A recognized leader in the profession announced a remedy, and the lesser lights accepted and prescribed it. One group used the so-called resolvent treatment; another held to purgatives and emetics, while some advocated the so-called enveloping remedies, mucilaginous and oily substances, the idea being to lubricate irritated parts and to catch or arrest in the viscous decoction the agent responsible for the disease. One group thought of the antispasmodics, such as valerian, musk and zinc oxide, as appropriate for whooping cough, while another group pledged its faith to narcotics and used chloral hydrate, opium and morphine. As the list of remedies lengthens, one finds what so frequently happens with empirical methods, or, if you please, with a plan of trial and error; the method which is highly praised by one group is berated and discarded by another. In the end most physicians were ready to agree with Heberden (1710-1801), who said: "There are indeed many remedies being flaunted everywhere for this disease, as is usual with illness in general, among which remedies there are none that are unfailingly effective."

It may be of some interest to mention, somewhat at random, various forms of treatment suggested by outstanding physicians of former times.

Baillou, considering whooping cough an unconquerable disease, advised an expectant treatment. Sydenham treated the convulsive cough of childhood with plasters, bleeding and repeated purges, though he was of the opinion that purgation should be mild. He recognized that the disease was obstinate and not readily curable. Willis recommended, in addition to the emetics and purgatives, a variety of musk; Ettmuller is said to have preferred a derivative of succinic acid, while Rosen von Rosenstein's (1706-1773) treatment consisted of applying three specifics in succession: marsh-rosemary against the "insects" of whooping cough miasma, seal fat for the suffocating spasm, and, finally, a mixture of tar and yolk of egg to do away with the remaining catarrhal cough.

William Cullen (1712-1790) also found whooping cough difficult to treat. In his opinion, nothing could be effective at the beginning, but later, when the disease continued from force of habit, active medication was to be employed to interrupt its course. For the early stages he prescribed bleeding and laxatives, blisters applied to the thorax to counteract the inflammatory tendency of the chest, and emetics, "imitating Nature," to shorten the paroxysms and make their return less frequent. He preferred antimony and potassium tartrate to the yellow sulphur of antimony vaunted by certain of his contemporaries. For the second stage Cullen's remedies were tonics—muscus pyxidatus, bark of oak, mistletoe, and Peruvian bark—and antispasmodics—castoreum, musk and hemlock. When the latter did not succeed he resorted to

opium, but found that even this powerful remedy did not entirely cure. Cullen also had a word to say about psychotherapy, anticipating Czerny who in recent years has expressed his belief that in many instances whooping cough depends on a neuropathic constitution. Cullen thought that "terror" might be a powerful remedy, but he found it difficult to measure. Recognizing that a slight degree may be ineffectual while a considerable degree may be dangerous, he hesitates to advise its use. A change of air, he finds, is not a specific.

Michael Underwood, who in 1797 wrote the most widely read book on children's diseases of his period, did not differ materially from his contemporaries in his directions for the treatment of whooping cough. To the usual remedies for "keeping the body open," he added tartarified antimony or its wine. As antispasmodics he used gum ammoniac and asafetida, camphor and castoreum. He thought that rubbing the hands and soles of the feet with compound spirit of ammonia, and the spine and the pit of the stomach with oil of nutmeg or oil of amber brought relief to his patients. Underwood believed that hemlock should be combined with other drugs. He did not believe that milk breeds phlegm, but he said that, should the milk curdle, salt or castile soap might be added. Underwood's treatment must have been effective, for though he boasted of having cared for many patients he knew of only one fatal case.

C. W. Hufeland, one of the German leaders in the early nineteenth century, divided the disease into a number of stages and gave directions for the treatment of each stage. The general treatment is, he stated, to cleanse the stomach, to calm the spasm with direct methods and counterirritants and to treat the complications. For the first stage, that of gastric catarrhal inflammation, the treatment should be resolving, cooling, laxative and emetic. For this he prescribed sodium and potassium tartrate, aqua foeniculi, syrupus mannae, squills, wine of antimony and extract of hyoscyamus. For the second stage, or paroxysmal period, he used hyoscyamus, asafetida, and belladonna by enema; in severe cough he gave opium, never continuously, however. As stimulants he advised musk and at times counterirritation by the use of inunctions with cantharides salve, tincture of camphor or an ointment made of antimony and potassium tartrate. He thought these remedies usually sufficed to cure the patient. The third stage is the asthenic period. The aforementioned remedies may not have been sufficient to stop the cough that has continued for several weeks. In some children paroxysms become less marked in consequence of increased weakness, and for these Hufeland recommended cinchona combined if necessary with some antispasmodic drug. If the cough continued with marked expectoration

of mucopurulent material, a preparation of iceland moss was thought to be the best remedy. During convalescence, for weakly patients lukewarm baths, cinchona, and iceland moss were recommended. Many physicians said of Hufeland, as was said of Galen in earlier days, "Hufeland says so, and, therefore, it must be that these remedies will cure the whooping cough."

At the beginning of the nineteenth century Jahn published a treatise on whooping cough which illustrates the theories of those who classed all diseases as either sthenic or asthenic. He explained that whooping cough takes either a sthenic or an asthenic form according to the diathesis of the patient. The fundamental principles of treatment were dependent on the various types of irritability, not at all on the nature of the infective agent, and, as Jahn pointed out, the type of infection in this disease was not known. The treatment, in other words, was "preservative" and planned so as to give the infectious matter time to leave the body. The remedies used for the various types of increased or depressed irritability include nearly the whole gamut of medicines known at the time, and in addition inhalations, clysters and baths.

C. M. Billard, one of the earliest French pediatricians, practiced in the early part of the nineteenth century. He found that two principal indications present themselves in the treatment of whooping cough; it is necessary, first, to combat the inflammation of the bronchi and, second, to remove nervous complications. He advised purging, bleeding, demulcent drinks and leeches to the neck or lateral parts of the thorax. Antimony and squills are used as expectorants, not as emetics. For the second indication he used narcotic and antispasmodic remedies—opium, syrup of poppies, asafetida by enema, hyoscyamus, belladonna and cicuta. He also mentioned a mixture of oxide of zinc, belladonna and cicuta. He used zinc oxide in doses of 1 grain (0.065 Gm.) every hour in an infant of 6 weeks with some success. He also mentions counterirritants and blisters.

Bouchut, the next eminent French pediatrician after Billard, considered prophylactic and dietetic measures of great importance. He advised avoiding cold and moisture but considered balmy and dry air beneficial. He recommended frequent small meals rather than large ones, and regarded isolation of the well from the sick as the only effective preventive measure. He thought that vaccination against smallpox shortened the duration of the disease and controlled the paroxysmal attacks. Demulcent drinks, foot baths and enemas were mentioned for use in the early stage. Venesection was advised only for sturdy children. In the second stage, mustard plasters or compresses of cold water and vinegar may be applied to the forehead if there is cerebral con-

gestion. The use of opium was deprecated, but that of belladonna was looked on with favor.

The teachings of Binz in the latter half of the nineteenth century were important for whooping cough therapy, for it was he who introduced the use of quinine for this disease. He favored the use of small doses given often at the beginning of the illness, followed later by larger doses at longer intervals. His preference was for the chloride rather than the sulphate of quinine.

All these leaders had many and enthusiastic imitators, though, of course, they had their violent opponents as well.

Enough has been said to indicate the great number of remedies which have been employed; it would be impossible and boring to name them all. Sedatives and antispasmodics of every known kind, good, bad and indifferent, have been used either internally or externally; inhalations of ether, bromide, ozone, hydrofluoric acid, carbon dioxide and hydrogen dioxide have all been tried at various times. Perhaps the most famous was the inhalation of illuminating gas. The treatment was popular twenty or thirty years ago. If a child fell ill with whooping cough, the parents were prepared, according to popular custom, to take the patient to the gas works. This was usually miles away and necessitated a long journey in the open air, which was of itself a good treatment. The children were taken into the gas works where they breathed the escaping fumes or the gas turned on by the obliging keeper. Usually the children became blue, weak and pale; though probably few were hurt by the treatment, certainly none was permanently cured.

It has already been mentioned that with the advent of the bacteriologic era therapy concerned itself chiefly with the destruction of bacteria. Inhalations of antiseptics attained vogue for whooping cough as well as for many other diseases. Carbolic acid, corrosive mercuric chloride and other antiseptic substances were employed for inhalation. Local applications to the pharynx and larynx soon became popular. Swabbing with cocaine, a solution of resorcinal or silver nitrate and insufflation of quinine, caffeine and boric acid, or sodium salicylate with sodium bicarbonate, have all been tried and rejected.

Nitric acid is one of the substances which enjoyed great popularity in the treatment of whooping cough for a short while. Arnoldi and Gibbs, in their treatise on whooping cough published in London in 1854, claimed that nitric acid cured whooping cough as effectually as quinine does intermittent fever. Yet a few years later Charles West spoke of this new remedy as already having fallen into comparative oblivion.

In the late eighties and during the nineties therapeutic fashion decreed that bromoform should be the remedy for whooping cough. It was a fairly useful sedative and antispasmodic, though it frequently

caused poisoning. Since it was not readily miscible with syrups and other vehicles it tended to float on the top of the mixture and, not infrequently, the patient received a teaspoonful instead of a few drops of bromoform. The medical literature of the time abounded with reports of bromoform poisoning. One scarcely hears this remedy mentioned today.

Various other treatments have had their advocates from time to time. Intubation has been tried, recommended and forgotten. Toward the end of the last century F. E. Manby of London pointed to fumigation with sulphurous acid as a measure which if at all generally employed would practically rid the world of whooping cough. T. W. Kilmer of New York City recommended the use of an abdominal belt firmly applied to the abdomen for supporting the patient while he coughed. This application certainly did no harm and probably gave the sufferer a sense of comfort and some support during severe paroxysms.

Physical therapy did not fail of trial; threats and punishments were sometimes resorted to. Children were pushed downstairs for the physical and mental effect it would have in curing the whooping cough. Hydrotherapy has, of course, had its share of attention.

Intramuscular injection of ether has been advocated in recent times, but it is a method that causes pain and sometimes abscesses. Rectal injections of ether in oil have been more successful in temporarily relieving paroxysms. Intramuscular injections of milk have also been thought effective.

Vaccination against smallpox has been used, and diphtheria antitoxin has also been advised. Lumbar puncture has been suggested for the treatment of obstinate cases.

It has been proposed in the treatment of the paroxysm to pull the jaw downward and forward, so as to interrupt prolonged and dangerous spasms.

There has hardly been a new discovery or invention introduced that has not been subjected to the method of trial and error in the treatment of whooping cough. Thus it was with roentgen therapy. Patients were given repeated roentgen treatments; according to reports, some of them seemed to show moderate improvement and some were slightly improved, while others showed no effect. The method has been occasionally revived, but those who have tried it are usually not seriously impressed with its efficacy.

Throughout all the years of treatment the search for the cause of whooping cough has continued with varying results. A small bacillus resembling Bacillus influenzae has been reported at various times as occurring in large numbers of cases of whooping cough. As early as 1887 Affanassieff isolated a streptobacillus from the bronchial secretion

of twenty of forty-nine patients with whooping cough. When injected intratracheally into dogs and cats this organism produced a typical paroxysmal cough. Czaplewski and Hensel found bacilli resembling influenza bacilli in a large number of cases of whooping cough. Similar observations were made by Spengler and others. In 1916 Bordet and Gengou reported that they had found a small nonmotile organism, rounded, sometimes ovoid and gram-negative. Neither capsules nor spores have been demonstrated. Bordet and Gengou found the organism during the catarrhal period and the first week of the paroxysmal stage of whooping cough. Bacillus pertussis, like the bacillus of influenza, is aerobic. Agglutination of Bacillus pertussis by serum from the patient during and after recovery from whooping cough occurs only irregularly.

Arnold Rich, writing in 1933 on the etiology and pathogenesis of whooping cough, throws doubt on the pathogenicity of the Bordet-Gengou bacillus. Briefly, he is of the opinion that an invisible virus may play a rôle in the etiology of pertussis. He believes that there may be a filtrable virus associated with pertussis capable of producing respiratory catarrh.

Opinion is divided. It is true that most clinicians and bacteriologists believe that Bacillus pertussis is the cause of the disease, but a number of investigators hold to the belief that a filtrable virus is the causal agent. Gundel and Schlüter [1] concluded from their recent studies that Bacillus pertussis is the specific cause of the disease. By cultural methods they were able to differentiate Bacillus pertussis from Bacillus influenzae. Genuine pertussis bacilli injected intracutaneously produced severe necrosis, while injection of influenza bacilli produced variable infiltration and erythema but never necrosis. Gundel and Schlüter believe that the complement-fixation reaction with pertussis bacilli in infected patients is characteristic, and, consequently, they say that Bacillus pertussis is the cause of the disease.

There is a voluminous literature on the subject of prophylaxis and treatment with vaccines. Sauer immunized about three hundred non-immune children. In the course of five years thirty-one controls (non-immunized children) contracted whooping cough, whereas twenty-nine immunized children who were actively exposed to the disease did not contract it. Sauer stated further that it requires four months to produce active immunity. From these data he believes that pertussis vaccine is not a curative agent but that it will actively immunize susceptible patients.

Convalescent serum has been advised for prophylaxis and treatment, particularly by a group of French clinicians. It has also been employed by Jundell, who used blood from adults with good results. Those in

1. Gundel, M., and Schlüter, W.: Klin. Wchnschr. **12**:1633 (Oct. 21) 1933.

authority are not in agreement as to the specific cause of this disease. Is one ready to draw final conclusions as to etiology, prophylaxis or treatment or destined to plod further along the path of trial and error in efforts to reach an adequate understanding of a disease which has baffled the attempts of medical men for four centuries? It remains the task of the historian of the future to write another chapter.

104 South Michigan Avenue.

Pediatric Biographies

JEAN FERNEL
1497?-1558

A NOTE ON THE HISTORY OF APPENDICITIS IN CHILDREN

JOHN RUHRÄH, M.D.
BALTIMORE

Jean Fernel, or Ioannes Fernelius, one of the outstanding lights of French medicine of the sixteenth century, was born, according to Mézeray, at Montdidier; according to Plancy, at Clermont. The date of his birth is also a question of dispute, 1497, 1485 and 1506 being stated. He went to Paris in 1516 to the Collége de Sainte Barbe, where he studied philosophy, mathematics and languages and received his M.A. in 1519. He continued to study with great zeal, but a quartan fever made him leave Paris, and this may have influenced him to take up the study of medicine. He taught philosophy in his alma mater while he studied for his doctor's degree, which he received in 1530. His devotion to mathematics almost ruined him financially, as he gave up most of his time to it. Finally, at the insistence of his father-in-law, as Fernel was spending his wife's dot, he devoted himself to practice, at the same time teaching medicine at the Collége de Cornuailles. He had a great vogue as a physician and made plenty of enemies, partly through his success. He was accused of not bleeding when it was indicated. While Henri II was yet Dauphin, Fernel was called to attend Diane de Poitiers. Henry wished him to devote his time to his family, but Fernel feigned pleurisy and got out of it. When Henri came to the throne he wanted Fernel for his private physician, but Fernel refused lest he oust the incumbent Louis de Bourges, but when Louis died, Fernel assumed the post, evidently to his dislike, for he had to travel with the king on his campaigns. On one of these Fernel took his wife along, and she fell ill and died. He was broken hearted and died not long after in 1558. He was buried in Saint Jacques.

Much has been written about Fernel. Among the stories is one that when he attended Marie de Medici, she thought that he, through his treatment, had made it possible for her to bear a child. She gave him an enormous fee and promised a like amount at the birth of each subsequent child.

While a medical student, Fernel, through his great interest in astronomy and his experiments, made the first exact measurements of the degree of the meridian.

He was a prolific writer, and Duret criticized him for not confining his studies to Hippocrates and for going in for the Arabians of Fernel's commentaries. Of the latter he wrote, "Faeces arabum melle latinitas condidit," which may be rendered "Arabian dregs preserved in Latin

Te ſol produxit dubia vt paradoxa valerent,
Senſibus vt liquidis arsque pateret Auûm.
Ingens Ferneli, τὸν καὶ φίρωλας ἄνδρα,
Orator, Phyſicus, Celſus & alter eras.

JEAN FERNEL
1497?–1558

honey." On the other hand, there are Latin verses in praise of Fernelius which are attributed to René Gervais and Nicolas Bourbon.

Two lines from a poem by Gervais are as follows:

> Hippocrates moriens arcanum credidit artis
> Fernelio: huic fama par fit et ingenio.

Hippocrates dying entrusted the secret of his art to Fernel: who became equal to him in fame and ability.

Of the many books written by Fernel the most important medically are: "Jo. Fernelii medicina," Paris, 1554; "Universa medicina," Paris,

1567, and "Therapeutice universalis," Lyon, 1569. All were reprinted several times. Fernel also wrote on surgery, pathology, pharmacy, venereal diseases, fevers, etc.

In the "Universa medicina" in book VI, chapter IX, of "The Causes and Signs of Diseases of the Intestines" there is to be found a short description of a case which is supposed to be the earliest description of appendicitis that has been found to date. The description seems clear. Fernel uses the expression "caecum intestinum" which was used by some authors for cecum and by others for appendix, or perhaps for both together. The case is of especial interest to pediatricians as the patient is a child.

CAUSES & SIGNS OF DISEASES OF THE INTESTINES
CHAPTER IX [1]

Closely related to obstruction is correction & narrowing of the intestines. This moreover may arise from the action of those things which are ingested: whether they be foods like bad quince, whether astringent clysters. Often from an impinging intestinal tumor of the mesentery or viscera: and this moreover is common. And it happens from an enterocele, when the intestine descends into the scrotum and is constricted there as if by a hand. And one of these cases is produced by the intestine itself, not by any other visible causes. It will not be out of order to mention in this place a memorable example.

A girl of seven afflicted with diarrhoea, passed for many days from the bowels a white, putrid and foul material, with no pain. The grandmother was tired of this daily flowing and to stop it took counsel with some other old women. In this case a quince as large as one's hand was secured and this the patient devoured, with the result that the stools were suppressed so that during the day and the following night nothing was passed. But with violent, most severe pains and cramps in the belly, she swelled up until the swelling suddenly became putrid. A physician came, who, suspecting the true state of affairs, tried first injections and mild clysters and then more severe ones to dislodge the noxious stinking material from the intestines and to ease the pain with fomentations: but in vain. Indeed with increasingly severe pains, repeated loss of consciousness and moreover with the vomiting of a fecal liquid she died miserably in two days. On opening the body the caecum intestinum [appendix?] was narrowed and constricted; also the quince was found adherent to the inside and stopping up the lumen, so that it absolutely could not pass through any other way: whence it happened that this acrid and corrupt material prevented from passing; the obstacle overflowing opened up itself an unusual route into the abdominal cavity, by a necrosis and perforation a little above the obstructed place; from whence in the gut just as by the outlet & the passage escaping it filled up the abdomen to its entire capacity. Hence the suffering of most severe pains, hence distension, hence loss of consciousness, the most cruel death following shortly the appearance of foul vomiting. This history will be of value to those who in an excessive flow of abundant and toxic fluid from whatsoever cause, hasten intemperately to stop & subdue it to the greatest misfortune to the patient.

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1. This translation is by Dr. Ralph H. Major in his "Classic Description of Disease" (Springfield, Ill., Charles C. Thomas, Publisher), and is used by permission.

Pediatrics in Art

CARE OF THE NEW-BORN

JOHN RUHRÄH, M.D.
BALTIMORE

One of Italy's architects and sculptors, Giovanni Pisano (about 1250 to 1330), who left a marked impress on that country's ecclesiastical buildings, did a number of church sculptures, including the famous pulpit in the cathedral at Pisa. It figures the birth of Jesus and the annunciation to the shepherds. The longer one looks at it, the more it

Sculpture by Pisano depicting the birth of Jesus and the annunciation to the shepherds.

intrigues the imagination. It contains, as do so many works of the period, two infants. One of these lies swaddled in the manger, and the two animals are regarding their visitor with mild surprise. The other child is about to be bathed in a stone basin of antique mold into which water is being poured from a finely wrought urn. The woman who is acting as nurse holds the infant on her right arm, while with her left hand she tests the temperature of the water.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

A Note on the Fractionation of Antimeningococcus Serum. P. P. Murdick and S. M. Cohen, J. Immunol. **24**:531 (June) 1933.

By means of experiments in protein fractionation the authors found that the agglutinative and precipitative activity of antimeningococcic serum was associated with the water-soluble globulin. This fraction was incompletely precipitated by 33 per cent of saturated ammonium sulphate. The separation was practically complete if the serum was dialyzed to remove electrolytes and diluted and the reaction adjusted to the point of maximum precipitation.

Fothergill, Boston.

The Lipoidal Content of Antipneumococcic Horse Serum. L. D. Felton and G. Kauffmann, J. Immunol. **24**:543 (June) 1933.

In a study of the lipoid content of antipneumococcic serum the authors found the lipoid content to be 27 per cent higher than in normal horse serum. There was no correlation between the lipoid content and the nitrogen content in either serum. There was no correlation between the lipoid content and protection, either in immune serums or in concentrated antibody solutions.

Fothergill, Boston.

Normal Flora of the Prepubertal Vagina. Horace Pettit and Charles H. Hitchcock, J. Infect. Dis. **53**:372 (Nov.-Dec.) 1933.

Pettit and Hitchcock summarize their observations as follows: "Studies of the prepubertal vagina in sixty children, most of whom had orthopedic conditions, show that the flora is predominantly diphtheroid in character. Gram-positive cocci, such as nonhemolytic streptococci and nonpigment-forming staphylococci, are present less frequently and in smaller numbers. Organisms of the intestinal flora seldom if ever occur in healthy children, though in severely ill patients there is a distinct tendency for them, together with Staph. aureus, to overgrow the normally occurring flora."

Toomey, Cleveland.

Excretion of Morphine by Normal and Tolerant Dogs. William A. Wolff, Cecilia Riegel and Edith G. Fry, J. Pharmacol. & Exper. Therap. **47**:391 (April) 1933.

Normal and tolerant dogs excrete about the same amount of morphine, 20 and 17 per cent. In each group about two thirds of the excreted morphine is recovered from the urine and one third, from the feces. These results confirm similar recent observations of others, in man as well as in animals, as against the early observations that morphine is largely excreted through the alimentary tract.

Pilcher, Cleveland.

Copper Content of the Blood of Infants. Carlo Currado, Pediatria **41**: 54 (Jan.) 1933.

The author gives a detailed review of the more recent studies on the biologic importance of copper, as well as on the content of this metal in milk and in blood. He submits the first results of his efforts in determining the content of copper in the blood of infants. In his work he followed the method of Schönheimer, Oshima and Elvehjem, and found that the average content of this metal in normal infants was 1.2 mg. per liter.

Signorelli, New Orleans.

CLINICAL INVESTIGATIONS ON BLOOD CATALASE IN NORMAL CHILDREN. URSULA KRÄTSCHELL, Arch. f. Kinderh. **100**:139 (Sept. 29) 1933.

In this report are tables showing the results of 144 quantitative blood catalase tests performed on 11 normal children of various ages. The rôle of blood catalase in the body's processes is discussed. LEMASTER, Evanston, Ill.

THE INTERNAL SECRETION OF THE SUPRARENAL CORTEX. ERNST SCHMITZ and J. KUHNAU, Biochem. Ztschr. **259**:301, 1933.

The two commercial preparations from the suprarenal cortex are not identical. Interrenin lowers the cholesterol and phosphatide of the blood of normal rabbits, whereas cortisupren lowers the cholesterol but raises the phosphatide content. In the case of B-avitaminosis of pigeons, interrenin inhibits the rise of the cholesterol, but may actually promote the fall in phosphatide; cortisupren inhibits both. From these facts it is concluded that the secretion of the suprarenal cortex must contain at least three components: a cholesterol-lowering, a phosphatide-lowering and a phosphatide-raising factor. The acetone extract of cortex material from beef suprarenal glands contains the phosphatide-raising substance A and the cholesterol-lowering substance B. An alcoholic extract of the dried residue from the acetone extraction contains the cholesterol and phosphatide-lowering substance C. A and B are separated by dilution of the acetone solution with water, extration with ether, evaporation, dilution with alcohol, saponification with sodium alcoholate—taking up the unsaponified material by evaporation with petroleum ether—and extraction with boiling sodium hydroxide. The component of A corresponds to $C_{25}H_{46}O_3$; it contains one hydroxyl group and one double bond. B corresponds to $C_{29}H_{50}O_3$, and also contains one hydroxyl group and one double bond. C has not been analyzed. These substances are thought to be part of a system regulating the sterol and phosphatide components and the fat metabolism in general. To establish that this regulatory mechanism is also responsible for the life-saving action, studies were also undertaken with the cortical preparation of Swingle-Pfiffner. The life-maintaining principle of the cortical preparation is identified with B. A and B are responsible for the powerful muscle reaction. B has been administered to patients with endogenous depression mania, which is characterized by hypercholesteremia, with favorable results. KUGELMASS, New York.

EFFECT OF THYMUS PREPARATION ON EXPERIMENTAL HYPERPARATHYROIDISM. H. G. SCHOLTZ, Ztschr. f. d. ges. exper. Med. **85**:547, 1932.

Administration of thymus extract to rats led to a fall in the serum calcium. Simultaneous administration of thymus extract and parathormone prevented a rise in serum calcium and decalcification of the bones. Splenic extract did not prevent parathormone hypercalcemia. KUGELMASS, New York.

Nutrition

THE VALUE OF BED REST IN THE TREATMENT OF MALNUTRITION. ROBERT A. BIER, Arch. Pediat. **50**:527 (Aug.) 1933.

The writer reviews his experience with a limited number of children at a farm for convalescent children and stresses the importance of rest in bed in the treatment of malnutrition. One hundred and seventeen patients were observed; of this number, fifty-eight regained their normal weight. The children receiving rest in bed gained weight much more promptly than those who were not so treated. Attention is called to the necessity of a follow-up study if the gain in weight is to be maintained. Etiology, symptomatology and treatment of malnutrition are considered.

WADDELL, JR., University, Va.

SUNSHINE AND IRRADIATED MILK THERAPY TO REDUCE HIGH INCIDENCE OF RICKETS. ESTHER B. HARDISTY, Arch. Pediat. **50**:549 (Aug.) 1933.

The relative merits of the various antirachitic measures now in use are discussed, and attention is particularly called to the value of irradiated milk in the prevention of rickets. Some of the more important contributions to the present fund of knowledge concerning rickets are reviewed.

WADDELL, JR., University, Va.

COD LIVER OIL CONCENTRATE. W. D. SUTLEFF, E. H. PLACE and S. H. SEGOVE, J. A. M. A. **100**:725 (March 11) 1933.

The use of cod liver oil concentrate (vitamins A and D) in daily doses of 100 minims (5.9 cc.) had apparently no effect on the incidence of otitis media in patients with scarlet fever.

BONAR, Salt Lake City.

THE SOY BEAN IN THE NUTRITION OF CHILDREN. GEORGE W. CALDWELL, M. J. & Rec. **138**:126 (Aug. 16) 1933.

The author gives a report of a clinical study of the use of soy bean flour as a supplement to the diet of sixty-six infants and children. He used the soy bean flour either mixed with cereal or in the milk or made with other ingredients into bread. The soy bean flour increases the caloric content and enhances the nutritive value of the foods. One ounce of the yellow soy bean flour equals 141 calories. The average gain of each child in the test group was 9⅘ ounces (266.49 Gm.) per month, as compared with an average gain of 6.7 ounces (189.95 Gm.) for each child in the control group. The soy bean is rich in protein and phosphorus and has a high calcium content.

WILLIAMSON, New Orleans.

IRON IN NUTRITION OF THE INFANT: III. IRON METABOLISM DURING THE FIRST YEAR OF LIFE. A. WALLGREN, Rev. franç. de pédiat. **9**:196 (Feb.) 1933.

These studies were made on five infants from 3 to 11 months of age, in Göteborg, Sweden, and complement those of Langstein and Edelstein. In agreement with these authors, Wallgren found a positive iron balance. The tables given for the elimination of iron at different months are of extreme interest and should be consulted in the original article. As an average, if the infant receives an amount of iron equivalent to 0.642 mg. per thousand grams, the needs of the organism will be fulfilled. This, therefore, can be maintained by human milk. In regard to the theory of the fetal iron depot, which was promulgated by Bunge and denied by Soxhlet, the author does not think that there is as much iron eliminated in the early months as is taken in. This would indicate a using and gradual withdrawal from such a fetal store.

SANFORD, Chicago.

THE NUTRITIVE VALUE OF WHEAT GERM. V. FAMIANI, Atti Accad. Lincei **16**:275, 1932.

The addition of wheat germ to whole wheat stimulates the growth of albino rats somewhat but does not make whole wheat a complete food, as the sexual functions particularly are not developed. The addition of 4 per cent of salts, however, causes almost normal development, only lactation being impossible. The addition of casein does not appreciably stimulate lactation.

KUGELMASS, New York.

CHOLESTEREMIA IN NORMAL BABIES AND IN BABIES AFFECTED BY VARIOUS DISEASES. A. SIMONINI, Clin. pediat. **15**:411 (June) 1933.

Cholesteremia in normal infants and in infants suffering from certain diseases, with special reference to cases of tuberculous infection, is the subject of this article. The author summarizes his conclusions as follows:

1. From birth through early infancy under normal (physiologic) conditions the new-born shows only slight variations in the cholesterol content of the blood.

2. In the presence of certain diseases the author was able to establish a real and evident parallelism between cholesteremia, organic resistance (of the patient) and the disease.

3. In infants suffering from various clinical forms of tuberculosis and in allergic conditions there was a demonstrable quantitative increase in cholesterol.

Since in all severe cases when the resistance of the body appeared to be overcome general hypocholesteremia existed, the author believes that the content of cholesterol in the blood serum of these patients represents an index of the defensive process (ability) of the body against disease.

SIGNORELLI, New Orleans.

METHOD OF DETERMINING THE BODY SURFACE AND ITS IMPORTANCE IN CALCULATING THE FOOD REQUIREMENTS OF THE INFANT. CONSUELO BARTALINI, Riv. di clin. pediat. **31**:591 (May) 1933.

The author made many measurements of the body surface of infants with the integrator and comparable calculations by the formulas of Lissauer ($S = 10.3\ W^{\frac{2}{3}}$) and of the DuBois brothers ($S = W^{0.425} \times H^{0.725} \times 71.84$). He believes that the DuBois formula is the more exact.

In calculating the caloric needs of a healthy child the determination of the number of calories per kilogram of body weight is a suitable, as well as a practical and simple, method. With overnourished or undernourished infants, the basis of calculating the food needed should be the body surface.

HIGGINS, Boston.

CHANGES IN THE INORGANIC AND ORGANIC PHOSPHORUS IN EXPERIMENTAL BERIBERI. A. LEONE, Riv. di clin. pediat. **31**:609 (May) 1933.

The phosphorus in the blood is diminished not only in vitamin D deficiency (rickets) but also in vitamin B deficiency (beriberi).

Nine pigeons were put on a diet deficient in vitamin B. When they showed the nervous symptoms, on the twentieth to the twenty-eighth day of the diet, blood was withdrawn and the serum was analyzed for the content of inorganic, organic (acid-soluble) and total phosphorus. The mean results are given in the following table.

	Inorganic Phosphorus, Mg.	Organic Phosphorus, Mg.	Total Phosphorus, Mg.
Pigeons			
Normal	3.6	6.3	9.9
With beriberi	2.0	3.8	5.8

In four instances the phosphorus was determined in blood obtained on intermediate days of the diet. On the fifth day the total phosphorus was 8.9 mg. per hundred cubic centimeters of blood; on the tenth day it was 7.60 mg. and 5.70 mg., and on the fourteenth day, 5.80 mg.

HIGGINS, Boston.

SIMPLE METHOD FOR THE STUDY OF THE PROPORTIONS OF THE DIFFERENT ENERGY FACTORS IN THE CHILD'S DIET. G. DE TONI and G. C. TAROZZI, Riv. di clin. pediat. **31**:906 (Aug.) 1933.

The authors give the tables of Camerer, Sundstrom, Tigerstedt, Holt and Fales and Terrien, with the recommended proportions of protein, fat and carbohydrate in the diets of children up to 14 years of age.

Their next tables give the number of grams of protein, fat and carbohydrate in varying weights of foods commonly taken by children. Thus in milk, cereal, soup and bread, figures are given for from 50 to 1,000 Gm.

From the figures given, the total protein, fat and carbohydrate in the child's diet is easily calculated. The proportions may be compared with the standards of the earlier tables.

HIGGINS, Boston.

THE MODIFICATIONS OF THE CREATINE METABOLISM IN AVITAMINOSIS: MODIFICATION IN EXPERIMENTAL SCURVY. G. A. PIANA, Riv. di clin. pediat. **31**:1098 (Sept.) 1933.

The author studied the creatine metabolism in guinea-pigs that were on a diet which would produce scurvy. The creatinine of the blood showed no definite change; it was diminished a variable amount. The elimination of creatine and creatinine in the urine was diminished especially during the period when the clinical manifestations of scurvy were present. HIGGINS, Boston.

THE p_H AND THE ALKALINE RESERVE IN CHRONIC NUTRITIONAL DISTURBANCES AND TOXICOSIS OF INFANCY. MAMERTO ACUNA and TELMA RECA, Arch. argent. de pediat. **4**:210 (June) 1933.

The authors made determinations of the p_H and the alkaline reserve in twenty cases of chronic nutritional disturbances and in ten cases of toxicosis. They consider as normal values a p_H of from 7.30 to 7.45 and an alkaline reserve of from 43.3 to 57.6. They found, contrary to the view held by Leenhardt and Burghi, no difference in the alkaline reserve of the breast-fed and the artificially fed infants. The mild dystrophies and dyspepsias did not seem to influence the acid-base balance as determined by the p_H and the alkaline reserve.

In the larger number of cases of toxicosis there was an acidosis, as indicated by a lowered p_H and alkaline reserve. No relationship was found between the degree of the acidosis and the severity of the toxic symptoms and the course of the disease.

The authors are of the opinion that although the antiacidosis treatment modifies and relieves the humeral state and the toxic symptoms derived from the acidosis, the clinical improvement and the recovery of the patient are not always concomitant with the reestablished acid-base balance. SCHLUTZ, Chicago.

RELATION OF THE BLOOD CHLORIDES TO TOXICOSIS IN THE INFANT. M. GERBASI, Arch. de med. inf. **2**:370 (Sept.) 1933.

The author reviews the literature on the studies of blood chlorides. Nothing in particular is added to the knowledge that chloropenia exists in the majority of infantile toxicoses. SANFORD, Chicago.

INFLUENCE OF PROGRESS IN NUTRITION ON INFANT MORTALITY. F. YGARTUA, Arch. de pediat., Rio de Janeiro **5**:373 (Sept.) 1933.

Ygartua discusses the recent advances in infant nutrition, such as scientific feeding, feeding of vitamin-containing foods and the newer treatment of intestinal disturbances. By such measures the infant mortality in Argi has been reduced from an average of 237 per thousand for the years from 1915 to 1925 to 176 per thousand by the end of 1932. SANFORD, Chicago.

CONDENSED MILK: ITS APPLICATION IN THE FEEDING OF INFANTS. O. MARTÍNEZ-FORTÚN Y FOYO, Bol. Soc. cubana de pediat. **4**:523 (Dec.) 1932.

About 70 per cent of the infants of the poorer classes are fed various preparations of sweetened condensed milk. If this is given intelligently after weaning, good results are obtained, and normal health may result. The author advises gradual weaning when condensed milk is used. In this way unfavorable results from this form of feeding may be avoided. It is more difficult to adulterate condensed milks than ordinary commercial cow's milk. On account of the large consumption of the product, it can usually be obtained in a fresh condition. It is good in cases in which cow's milk is not well tolerated. It is useful in conditions of hypotrophy and hypertrophy and is well taken by infants who are troubled by persistent vomiting or a tendency to diarrhea. SCHLUTZ, Chicago.

APPLE DIET IN THE TREATMENT OF INFANTILE DIARRHEA. J. M. GONZÁLEZ GALVÁN, Paidoterapia **12**:229 (July) 1933.

The apple diet represents a simple, efficient method lacking counterindications in the treatment of infantile diarrhea. The diarrhea is usually abated within a short time, and this makes the treatment adequate for the acute and grave forms of infantile enteritis. It is a revolutionizing remedy which will make one forget the old complicated methods that necessitated a diagnostic, clinical and laboratory selection.

In forty-two of forty-three cases reported the diarrhea was cured by this treatment.

HERRON, Spokane, Wash.

CRITICAL REVIEW OF THE MODERN TREATMENT OF THE HYPOTROPHIC INFANT. JULIO LOPEZ LOMBA, Rev. méd. latino-am. **13**:664 (March) 1933.

This extensive review does not consider athrepsia a fatal involvement in the majority of instances as used to be the case, but places a good prognosis on the average case. Up to ten years ago the treatment consisted in employing a rational diet, in prescribing, without much enthusiasm, many preparations such as lecithin, phosphorus, calcium, iron and arsenic, and in injecting artificial serums. The hypotrophy, the cause of which is syphilis, is now treated as a syphilitic involvement. There is no difference in the treatment of the infant with symptomatic and the one with essential hypotrophy.

The treatment is divided into five groupings:

1. Dietetic treatment consists of the rigorous regulation of the quantity, quality and regularity of the meals, always keeping in mind the age, weight and state of the digestive functions of the child, since the tolerance for food is lowered, so that it is not possible to give the quantities of food that correspond to the age or weight of the child. Breast milk is preferred, but if there is an intolerance for it, then Lomba prefers the milk of the burro, or goat's milk. The milk must contain a high caloric value in relation to volume, so sugar is added up to 30 grains (1.95 Gm.) per kilogram a day. The milk can be concentrated to a half or a third. Water is given between feedings. In infants over 4 months of age the pudding diet of Moll and Stransky can be used. If mucus accumulates in the stomach, Lomba resorts to lavage, which rapidly stops the vomiting and acts favorably on the diarrhea.

2. The establishment of the water equilibrium of the cells is an important phase of the treatment. The use of serums, hypertonic salt solutions or isotonic salt solutions is not justified until a study has been made of the alkali reserve, serum chlorides and blood nitrogens. When there is diminution in the serum chlorides with uremia, saline solution should be given, but when there is a retention of chloride with uremia, dextrose solution should be given.

3. Physical therapy avoids the use of either moist or cold air. Air at 26 C. (78.8 F.) is best. Crying is good for the child, because it is a sort of breathing exercise. Ultraviolet irradiation and diathermy are of value.

4. Sulpharsphenamine is of value only in the cases in which syphilis is diagnosed.

5. Medications of biologic origin are varied. Four cubic centimeters of mother's milk should be injected subcutaneously three times a week and continued until the child's condition improves. Asepsis must be used rigorously. From 5 to 10 cc. of human serum should be injected at frequent intervals. Insulin is employed, preferably in children over 1 year of age. The dose is 1 unit per kilogram of body weight, which can progressively be raised in some cases to 3 or 4 units per kilogram, followed by the oral administration of at least 3 Gm. of sugar for each unit injected. Lomba prefers to give the entire insulin dosage at one time, but a careful lookout for insulin shock must be made. This treatment is continued for from two to three months, at the rate of fifteen or twenty injections a month. In twenty autopsies, no important changes were noted in most of the organs; but degenerative areas were found in the thyroid gland in all cases. Thus, extract of the thyroid gland has been administered with good results.

Finally, the variety and efficacy of any treatment depend on the proper application of the treatment after careful study has been made of each individual case.

HERRON, Spokane, Wash.

EFFECT OF THE APPLE DIET ON THE NITROGEN AND MINERAL METABOLISM. HERBERT HÜTKER, Arch. f. Kinderh. **100**:2 (July 18) 1933.

Experiments in metabolism were conducted on five children from 7 to 10 years of age, who received the raw apple diet. During the apple regimen the nitrogen balance was negative, and the nitrogen level of the blood serum was lowered. The sulphur, phosphorus and calcium balances were also negative. The literature on this subject is reviewed. The author states that clinical observation indicates good results without exception from the use of the apple diet in acute and chronic, enteral and parenteral digestive disturbances and in nephritis with elevated blood nitrogen.

LEMASTER, Evanston, Ill.

DETERMINATION OF VITAL CAPACITY IN CHILDREN BY THE ESTIMATED BASAL METABOLISM. E. PUSCHEL, Monatschr. f. Kinderh. **58**:280, 1933.

The writer reviews the literature concerning the various efforts made to determine vital capacity by means of body measurements. The more recent studies are concerned with basal metabolism in reference to vital capacity. He then includes various tables submitted by other authors and studies of his own.

In sixty-eight children, aged from 5 to 16 years, the basal metabolism was estimated according to the tables of Kestner and Knipping. Dividing the vital capacity by the metabolism gives a certain quotient. Puschel finds that this quotient is somewhat lower in children than it is in adults.

He concludes that the vital capacity has no definite relationship to basal metabolism.

GERSTLEY, Chicago.

TOXIC EFFECTS OF IRRADIATED STEROLS. B. KELLNER, Virchows Arch. f. path. Anat. **288**:491, 1933.

The histologic effects of irradiated sterols were studied in two series of fully grown young rats comprising, respectively, 85 and 130 animals. It is of interest that crystalline viosterol was found to be nontoxic in the first series of animals, although the substance was therapeutically active in rickets in man. This led to a study of the daily dosage of several irradiated sterols of ergot origin necessary to cause toxic effects. Subtoxic doses caused no histologic changes when continued for a long time, even half a year. The toxic effects noted were those previously described, namely, degeneration and necrosis followed by calcification. The kidney and aorta were most frequently affected. The peripheral arteries, heart muscle and voluntary muscle came next. In the bones toxic doses led to the formation of osteoid tissue, followed in some animals by hypertrophic changes in the bones and in others by atrophic changes, the latter being noted especially with the larger doses or a more prolonged administration.

SCHULTZ, Evanston, Ill. [ARCH. PATH.]

THE ANTISCORBUTIC ACTION OF ASCORBIC ACID. JOHANNES BRUGGEMANN, Ztschr. f. physiol. Chem. **216**:139, 1933.

A preparation of ascorbic acid from hawthorn was tested on guinea-pigs. Scorbutic animals receiving a daily dose of 666 microns showed distinct improvement, and those receiving 800 microns or more were completely cured.

KUGELMASS, New York.

FREE FATTY ACIDS IN COD LIVER OIL VITAMIN D. O. K. SCHULTZ, Ztschr. f. Vitaminforsch. **1**:287, 1932.

Six samples of oil containing from 1 to 20 per cent of free fatty acids were tested on rats for vitamin D (I) over a period of two years. The loss in potency was the same (approximately 30 per cent) for all the oils, indicating that the free fatty acid content does not influence the stability of its I. With the exception of bleaching no method of commercial preparation influences the I content.

KUGELMASS, New York.

Prenatal Conditions

CERVICODORSAL SPINA BIFIDA. G. DARCOURT, Bull. et mém. Soc. de chir. de Marseille, Oct., 1932, p. 319.

A 4 year old girl was afflicted with a large spina bifida in the cervical region. The protrusion was at the nucha, was of the size of a large orange, had regular ridges, and was partly reducible, but its reduction caused a distressing headache. Roentgenography showed it to include the last two cervical and the first three dorsal vertebrae. There was also revealed a spina bifida occulta at the fifth lumbar vertebra.

VINTON, Brooklyn.

A RARE CASE OF PELVIC MEGACOLON. GEORGES ROSENTHAL and CONSTANTINESCOU, Bull. Soc. pédiat. de Iasi **3**:97 (Oct. 31) 1932.

A case of extreme dilatation of the sigmoid colon in a boy aged 9 years is reported. Severe constipation had been present since the first few weeks after birth. The general physical development of the boy was good. Roentgenologic examination following the administration of barium sulphate by mouth showed no abnormality. However, when barium was introduced by rectum, 3.5 liters was injected before the child complained of discomfort. When distended the sigmoid colon filled a large part of the abdominal cavity. The medical and surgical treatment of this condition is briefly discussed.

LEMASTER, Evanston, Ill.

THE FEEDING OF PREMATURE AND NEW-BORN INFANTS WITH CONGENITAL DEBILITY. A. B. MARFAN, Paidoterapia **12**:651 (Nov.) 1933.

Congenital debility is most common in premature infants, but all premature infants are not weak. On the other hand, many infants born at term show congenital debility and are immature. For infants with congenital debility breast milk is absolutely the best food. If the immature or premature infant is able to nurse he should suckle the breast. If the mother does not have sufficient milk, a wetnurse is advisable. If syphilis is suspected the infant should be fed the breast milk from a bottle or a spoon. When a sufficient amount of breast milk is not available, "milk serum" combined with breast milk is good. If artificial feeding is necessary from the first, the prognosis is not nearly so good. The milk of the ass is preferred, and when this is not available a partially skimmed milk with carbohydrate added is used. A feeding is offered every three hours, and if the infant is too weak to be fed from a bottle feedings with a dropper or by gavage are used.

HERRON, Spokane, Wash.

VIABILITY OF PREMATURE INFANTS. HELÉNE FISCHER-BÁN, Klin. Wchnschr. **10**:1354 (July 18) 1931.

The survival of an infant, born prematurely, 6½ months, weighing 600 Gm., is reported. The previous low weight record with survival stood at 680 Gm. The infant was given teaspoonful doses of tea for the first twelve hours of life and after that a teaspoonful of breast milk every two hours. From the eighth day a bottle was given, and the child was put to breast at 3 months.

The author states that premature infants weighing over 1,200 Gm. are put to breast or are given breast milk either from the bottle or with a teaspoon; if necessary, gavage is employed. Infants weighing under 1,000 Gm. are seldom strong enough to nurse, or else they tire very easily; the sucking reflex may not be well developed, and the pharyngeal reflex is also underdeveloped, so they may easily aspirate the food. The author advises complementing mother's milk so as to supply from 150 to 200 calories. She states that the mental development of premature children is slower than that of infants at term, but that later compensation takes place.

SILVERMAN, Syracuse, N. Y.

UNUSUAL INSTANCE OF POLYDACTYLISM. M. MIKULA, Bratisl. lékar. listy **13**: 208 (May) 1933.

A boy, aged 3½ years, had twenty-six well developed digits. He was remarkably fat and had diminutive external genitals, somewhat deficient intellectual faculties, strabismus, and retraction of the visual fields. On his right hand, the third metacarpal bone was uncinate, each prong supporting a complete phalanx; the fifth metacarpal bone gave attachment to two fully formed but stubby phalanges. On the left hand, an additional and shorter phalanx grew from a diminutive metacarpal bone attached to the mesial aspect of the fourth metacarpal, and a phalangeal stub with three centers of ossification sprang from the fifth metacarpal bone. Each of his feet carried six toes. Polydactylism with adiposogenital dystrophy constitutes the Bartlett-Biedl syndrome. In this patient retinitis pigmentosa and the tower head were lacking to complete the picture of the syndrome.

VINTON, Brooklyn.

CARDIAC ANOMALIES. F. KLEIN and J. LADENYI, Bratisl. lekár. listy **13**:219 (May) 1933.

In a girl who died at 1 month of age the following anomalies were found: In the right auricle, immediately below the opening of the superior vena cava and between it and the tricuspid valve there was a depression, a vestige of the upper portion of the right valvula venosa. The fossa ovalis was patent. The right ventricle presented a great multiplication of the papillary muscles, and its middle portion was rudimentary. The pulmonary artery had only two valves, the right and the left. These valves were unable to contract as far as Vries considers normal (*Beitr. z. path. Anat. u. z. allg. Path.* **64**:39, 1917) because of a raphe on one and because of the equal length of both. The ventricular septum presented two openings, the upper, 11 by 8 mm., the other, 16 by 11 mm. The left auricle had three pulmonary veins. In the left ventricle there was a multiplication of papillary muscles with marked trabeculation.

The upper opening of the ventricular septum, located above the excitoconductor system and including the entire membranous portion of the auriculoventricular septum, resulted from failure of the inferior aorticopulmonary septum to unite with the intermediate septum of His. In plain words, there was an extensive subaortic opening. The lower opening, also located above the excitoconductor system, could not be called intertrabecular, according to Sato's researches, as when situated below that system. Such a double hiatus has never before been described. The authors ascribe the formation of the lower system to failure of union between the intermediate septum of His and the ventrocaudal portion of the inferior septum because of aplasia of the latter.

VINTON, Brooklyn.

CHONDRODYSTROPHIA FOETALIS DIAGNOSED BY ROENTGEN EXAMINATION BEFORE DELIVERY. N. E. CRONBERG, Acta obst. et gynec. Scandinav. **13**:275, 1933.

Roentgen examination plays an important rôle in the diagnosis of fetal positions, which palpation alone cannot fill, and throws light on certain fetal deformities. A case is described in which roentgen examination of a pregnant woman imme-

diately before delivery revealed a fetus exhibiting such alterations that there was every reason to suppose it was a case of chondrodystrophia foetalis. This is the first reported case of this condition in which the diagnosis was made by roentgen examination before delivery. The woman, 43 years of age, came to the hospital in labor at term suspecting that she might have twins owing to the very large size of the abdomen. She had had ten normal deliveries, one of twins. The children were all normal in every respect. She was known to have had a cardiac condition for years, with palpitation and dyspnea during exertion. The abdomen was large and palpations were difficult. The inlet of the pelvis was empty as revealed by abdominal and rectal examination. The heart tones were heard on both sides of the abdomen. To rule out the possibility of a twin pregnancy a roentgenogram was taken, which showed breech presentation of an infant with an enormous head out of proportion to the size of the body, the head with density of calcium and lack of visible sutures between the bones of the skull. The limbs appeared short, thick and deformed, with irregularly thickened bone extremities. Spontaneous delivery seemed beyond the range of possibility, owing to the large calcified head with breech presentation, and it appeared that even craniotomy would be difficult. In view of these facts, cesarean section was performed, and a very large child weighing 4,660 Gm. was extracted. The baby was cyanotic, weak and pale, and died fifteen minutes after delivery. The cranial circumference was 10 cm. greater than normal. No sutures could be felt, although the anterior fontanel was plainly palpated. The head was very hard and could not be compressed by strong pressure. The limbs were very short. Roentgen examination in this case was very valuable in determining the obstetric procedure and establishing a prenatal diagnosis.

FAHEY, Chicago.

Diseases of the New-Born

BLEEDING IN THE NEW-BORN. F. H. CLARK, Arch. Pediat. **50**:482 (July) 1933.

Fifty cases in the writer's private practice are reviewed and conclusions are presented:

"1. The morbidity of bleeding in the new-born has increased in recent years because of more rigid inspection. All new-borns should be inspected daily during the first week.

"2. Infants born of mothers in the age group of 35 to 42 have a somewhat greater tendency to bleed.

"3. First born infants have a somewhat greater tendency to bleed.

"4. Chloroform anesthesia is negligible as a factor in the morbidity but is a significant factor in new-born bleeding mortality and in general new-born mortality.

"5. Prolonged bleeding and coagulation times are not observed as frequently as formerly.

"6. Melena may occur without an increase in the bleeding and coagulation time.

"7. The term 'oozing time' is suggested to replace 'bleeding time.'

"8. Fever is not to be dismissed lightly in the new-born, and all cases with fever should be especially watched.

"9. Atelectasis favors the bleeding tendency.

"10. Cerebral hemorrhage favors the bleeding tendency.

"11. Bleeding in the new-born is becoming a milder syndrome.

"12. Palatal petechiae are an early diagnostic sign.

"13. Asphyxia increases the bleeding time and is an etiological factor in a certain number of cases of idiopathic hemorrhagic disease, particularly with high bleeding times and normal or near normal coagulation times.

"14. The effects on the bleeding tendency in the new-born period of pressure, asphyxia, atelectasis and of toxins, such as chloroform, are appropriately expressed by the term anoxemia.

"15. Anything contributing to anoxemia, including cerebral injury, asphyxia neonatorum, atelectasis, and the toxins of some types of septicemia, affects adversely the bleeding time.

"16. Allergy may prove to be the etiological factor in some cases.

"17. The terms true or idiopathic hemorrhagic disease will be used to define a steadily diminishing number of cases as the etiological factors become more clearly understood.

"18. Bleeding in the new-born is a syndrome that may be incited by different factors and combinations of factors."

WADDELL, JR., University, Va.

TETANY IN THE NEW-BORN. HERMAN L. MASLOW, Arch. Pediat. **50**:768 (Nov.) 1933.

Maslow reports five cases considered by him to be instances of tetany, all of which occurred in new-born infants. All the patients on admission had a serum calcium lower than 7.5 mg. per hundred cubic centimeters. Electric reactions are not recorded. Four of the patients had an increase in the inorganic serum phosphorus. In one case the tetanic symptoms proved very resistant to intensive treatment with calcium and vitamin D milk; parathyroid extract was effective in raising the serum calcium. Maslow suggests that in this case the condition may have been due to dysfunction of the parathyroid glands. He discusses other suspected cases reported in the literature. He believes that tetany of the newly born is more common than one supposes, although somewhat atypical in its manifestations.

WADDELL, JR., University, Va.

ABDOMINAL CATASTROPHES OF THE NEW-BORN. W. H. CRAWFORD and R. M. TYSON, Arch. Pediat. **50**:784 (Nov.) 1933.

Crawford and Tyson review the records of 4,172 births at the Philadelphia Lying-In Hospital and report the occurrence of ten abdominal catastrophies in this group of infants. The rate of occurrence was about 2.4 per thousand births. Most of the catastrophes were traced directly or indirectly to congenital anomalies; a fairly large percentage were due to injuries received at birth and a smaller percentage to neoplasms.

The cases included two of hemorrhage into the peritoneal cavity, and of gastric ulcer ruptured on the eighth day, two of peritonitis and five of intestinal obstruction. The latter were due to (1) malposition of the stomach, (2) atrophy of the duodenum, (3) retroperitoneal hernia, (4) strangulated inguinal hernia and (5) imperforate anus.

WADDELL, JR., University, Va.

RUPTURE OF THE LIVER IN A NEW-BORN. HENRY S. MEYER, Arch. Pediat. **50**:814 (Nov.) 1933.

Meyer reports a case.

WADDELL, JR., University, Va.

RESUSCITATION OF NEWLY BORN BABIES SHOWING NARCOSIS. EVAN SHUTE and M. EDWARD DAVIS, Canad. M. A. J. **29**:252 (Sept.) 1933.

Three hundred and twenty infants delivered after the administration of morphine to the mother were observed. One hundred and twenty showed some degree of narcosis. Twenty-five of the 120 showed deep narcosis. Thirty-six babies were resuscitated with carbon dioxide or oxygen or mixtures of both. In 84 cases no gases were used for resuscitation. Two of the 36 for whose operations gas was used died, and 8 of the 84 for whose operations no gas was used died. Excluding premature babies weighing less than 2,500 Gm., the mortality was 4.3 per cent.

Pure carbon dioxide alone, pure oxygen alone, 5 per cent carbon dioxide with oxygen, 10 per cent carbon dioxide with oxygen and 30 per cent carbon dioxide with oxygen were used.

Pure carbon dioxide used for three or four gasps, followed by pure oxygen for a few moments, was found to be the most effective method. For general clinical use a 10 to 30 per cent mixture of carbon dioxide in oxygen is recommended. The simplest type of apparatus, a mask fitting tightly over the child's face, is used.

The literature on resuscitation with gas and the physiology of respiration in the newly born are considered briefly.

MOORE, Omaha.

PREVENTION OF NEO-NATAL MORTALITY. ALAN BROWN, Canad. M. A. J. **29**: 264 (Sept.) 1933.

It has been estimated that at least 40 per cent of the deaths during the first year of life occur during the first month. One third of the 40 per cent occur during the first day of life.

It is believed that this neonatal mortality can be reduced. Between June 1, 1931, and June 1, 1932, at Toronto General Hospital, there were 1,006 births, with a neonatal mortality of only 18. This probably represents the irreducible minimum.

There are four main indications for the physician in the reduction of neonatal deaths: (1) more extensive employment of the natural feeding of infants; (2) improvements in the artificial feeding of infants; (3) prevention of respiratory diseases in the new-born and (4) prenatal and postnatal supervision.

Breast feeding is especially emphasized by the author.

MOORE, Omaha.

STREPTOCOCCIC SEPTICEMIA OF HEMATOGENOUS ORIGIN IN A NEW-BORN INFANT. J. A. RITTER and N. RALPH, J. A. M. A. **101**:771 (Sept. 2) 1933.

Cyanosis developed the morning after birth and the infant died a few hours later during a profuse hemorrhage from the nose and mouth. From the cultures of consolidated blood taken from the lung and heart two hours after death a pure growth of Streptococcus haemolyticus was obtained. Toxic changes were noted in the viscera, and marked hemorrhagic pneumonitis was present. Cultures of the blood of the mother, who had had chills, fever and sore throat before delivery, showed a similar organism. The mother died on the eighth day post partum. The bacteriologic studies lead Ritter and Ralph to class this as a case of septicemia of hematogenous origin, probably by way of the placental circulation.

BONAR, Salt Lake City.

POSITION OF GERMS OF DECIDUOUS TEETH AT BIRTH. A. MARTIN SCHWARZ, J. Dent. Research **13**:217 (June) 1933.

The position of the deciduous incisors in both jaws at birth varies about fifty grades between protrusion and retrusion. Early in the embryonic development the germs of deciduous teeth lie in a row without lack of space, those of the lateral incisors being disposed somewhat orally from the first incisors. If, later in life, lack of space occurs, these teeth are affected first. They then lie most orally from the other teeth and also are turned. Central and lateral incisors on each side lie first in a common bony alveolus, indicating a close relationship in development. The wide shape and regular arrangement of the germs of deciduous teeth without lack of space and without torsion are an expression of undisturbed intra-uterine development and of harmony between the growth of the teeth and the jaw bone.

AUTHOR'S SUMMARY.

RESEARCHES UPON THE PREVENTION AND TREATMENT OF ASPHYXIA IN THE NEWBORN. LOUISE MCELROY, M. J. & Rec. **138**:341 (Nov. 15) 1933.

This article is part I of a series and has for its subject the intranatal causes of asphyxia. The direct cause of fetal asphyxia in labor, McElroy states, is some interference with the supply of oxygen from the maternal to the fetal blood or excessive retention of carbon dioxide in the fetal blood. She then gives the different

conditions that may cause this change in the blood. She divides the main causes of asphyxia into two classes: (1) suffocative and (2) paralytic. As suffocative causes she gives: (1) compression of the uterus when the labor is severe or prolonged enough to have a harmful effect on the fetal circulation; (2) pressure on the cord; (3) separation of the placenta; (4) prematurity, and (5) sedative drugs administered to the mother. As paralytic causes, she discusses intracranial injuries and the factors that contribute to these injuries. She gives the findings of some research workers whom she directed in examining stillborn infants.

WILLIAMSON, New Orleans.

TETANY CALCIPEXICUS OF THE NEWBORN INFANT. ALLAN BLOXSOM and H. O. NICHOLAS, South. M. J. **26**:883 (Oct.) 1933.

Two cases of spasmophilia of the new-born infant are reported, with high diffusible calcium and an apparently low concentration of ionizable calcium in the blood serum of one infant that was completely studied. Introduction of more calcium ions reduced the diffusible calcium concentration, increased the total calcium concentration and resulted, as far as can be determined, in a complete recovery of the neuromuscular irritability of the infants.

Attention is called to the possible difference in the production of this type of spasmophilia occurring in these new-born infants who had symptoms similar to classic tetany and of the spasmophilia producing tetany in older infants. It is believed that there is a substance present in the blood serum of the mother and infant preventing ionization of the diffusible calcium in the new-born and that this substance is produced in the placenta.

Diffusible calcium values must not be interpreted as meaning the total calcium available physiologically for the control of neuromuscular irritability. A working hypothesis is offered to explain the mechanism for the production of tetany in all cases. It is suggested that spasmophilia in the new-born infant associated with an increased diffusible calcium be termed tetany calcipexicus of the new-born infant, indicating a binding or making fast of the diffusible calcium ions. This term will serve to differentiate the type of tetany reported here from the tetany of older infants, tetany caused by hyperventilation and tetany parathyreopriva.

SCHLUTZ, Chicago.

ICTERUS GRAVIS NEONATORUM. ROBERT HUTCHINSON, Proc. Roy. Soc. Med. **26**:1268 (Aug.) 1933.

The patient, an infant of 21 days, was the second child. The first child was healthy and showed no sign of icterus. The patient was well nourished. He was somewhat drowsy. The liver and spleen were enlarged. The condition of the patient was improved by a transfusion of blood. The blood counts and laboratory tests are given in the report.

WILLIAMSON, New Orleans.

THREE TYPES OF HEMOLYTIC ANEMIA IN THE NEWBORN. HELEN MACHAY, Proc. Roy. Soc. Med. **26**:1360 (Aug.) 1933.

The author reported two cases of true hemolytic anemia in the new-born, or severe anemia without jaundice, one case of hemolytic anemia with icterus gravis neonatorum of familial type and one of hemolytic anemia in the new-born presumably caused by an intestinal infection and hepatitis. The reports include the family and clinical history, examinations of the blood and treatment.

WILLIAMSON, New Orleans.

SEVERE ANEMIA IN A NEWBORN CHILD. JEAN SMITH, Proc. Roy. Soc. Med. **26**:1372 (Aug.) 1933.

This case was reported in a girl 9 weeks of age. The red cell count was 800,000 and the hemoglobin 18 per cent when the first count was made. The baby received two blood transfusions while in the hospital, after which a colloidal iron

preparation was given twice a day for ten days; the blood count showed great improvement. The baby was given a mixture containing iron and ammonium citrate and was discharged. Two months later the red cell count was over 4,000,000 and the hemoglobin was 76 per cent. Full descriptions of the blood pictures accompany the report.

WILLIAMSON, New Orleans.

CONGENITAL UMBILICAL HERNIA. SILVESTRE LUIS SALA, Arch. méd. d. Hosp. Ramos Mejia, Buenos Aires **15**:166 (April) 1933.

The case was that of an infant weighing 3,700 Gm. The sac containing the intestines and mesentery measured 15 by 18 cm. in circumference. It was irreducible. An operation was performed within the first twenty-four hours and the child recovered.

SANFORD, Chicago.

INTRACRANIAL HEMORRHAGE IN THE NEW-BORN. VICTOR SANTAMARINA, Arch. de med. inf. **2**:347 (Sept.) 1933.

Intracranial hemorrhage in the new-born is due to the following causes: instruments, protracted delivery, prematurity and hemorrhagic disease (the author here refers to the secondary type due to syphilis). The symptoms may be divided into two types: those of the supratentorial type are pallor, whining cry, restlessness, lack of deglutition, muscular spasticity, tonic-clonic convulsion, bulging fontanels, difficulty in respiration, hemorrhage and xanthochromic spinal fluid; among those of the infratentorial type are drowsiness, cyanosis, asphyxia, bradycardia, nystagmus, depressed fontanel, slight convulsions and decreased deglutition. From a pathologic standpoint the supratentorial type shows a dilatation of the vessels covering the brain, with extravasated blood which forms a compact clot. The infratentorial type shows extravasated blood which is not coagulated. The treatment consists of lumbar puncture, an ice-pack to the head, calorifics, an alkaloid from lobelia, calcium bromide, calcium chloride, maternal blood and milk by dropper.

SANFORD, Chicago.

DISEASES OF THE LUNGS IN THE NEW-BORN, ASSOCIATED WITH THE ASPIRATION OF AMNIOTIC FLUID. FRANZ SZLÁVIK, Beitr. z. path. Anat. u. z. allg. Path. **89**:40, 1932.

Aspirated amniotic fluid is commonly found in the lungs of the new-born. The anatomic findings following aspiration of the fluid depend on the chemical constituents and the amount of aspirated fluid, the duration of birth and the length of extra-uterine life. They consist in a more or less severe inflammation of the pulmonary tissue, which by itself, however, is never fatal, but heals as a rule within the first week. Aspiration of infected fluid was observed in a stillborn child, the mother having died of streptococcic metritis. Infection of the lungs in the new-born can be due to aspiration of vaginal secretion during birth, by aerogenous infection or by the aspiration of vomitus. It may lead to fatal lobular pneumonia. In one of the author's cases the pneumococcus type IV was the infecting organism. Fetal atelectasis is recognized by the presence of myelin in the alveoli. It forms from degenerated alveolar epithelium.

HELLWIG, Wichita, Kan. [ARCH. PATH.]

GONOCOCCIC SEPTICEMIA IN THE NEW-BORN. B. SODERLING and S. FENLEN, Finska läk.-sallsk. handl. **75**:856 (Sept.) 1933.

The authors report a case of gonococcic septicemia in a new-born infant (hematogenous intra-uterine infection), the mother having an active gonorrheal infection. The main symptoms were multiple arthritis with swelling, tenderness and partial ankylosis and septic temperature. Roentgenologic findings of periostitis and positive complement fixation supported the diagnosis.

ELGHAMMER, Chicago.

Acute Infections

"Brucellin": A Possible Specific in Undulant Fever in Man; Preliminary Report. I. Forest Huddleson and Howard W. Johnson, Am. J. Trop. Med. **13**:485 (Sept.) 1933.

The authors discuss briefly the various procedures employed in making a diagnosis of undulant fever and give their method of arriving at the correct diagnosis. They describe the preparation of brucellin, a filtrate made from the beef liver infusion broth of the three species of Brucella, and report the cases of twelve patients treated with this preparation. They found that if the diagnosis was made early and treatment with the filtrate instituted, the condition both in children and in adults responded readily to this treatment, whereas in the late cases there was little or no improvement.

Burpee, Augusta, Ga.

Modified Quarantine in Measles Epidemics. Reuben Steinholz, Arch. Pediat. **50**:455 (July) 1933.

In order to avoid prolonged quarantine as a result of outbreaks of measles in a children's hospital a modified quarantine was found to be practical and useful.

"1. Transfer the case to a contagious disease hospital.

"2. Inject all children on the ward, except those having had measles, with 40 cc. of whole blood obtained from one of the parents.

"3. Admit cases to the ward that have had measles as shown by a doctor's certificate.

"4. Admit other cases to the ward after receiving an injection of 40 cc. of whole blood intramuscularly.

"5. Permit discharges of those that have had measles as shown by a doctor's certificate.

"6. No cases that have received whole blood injections are to be discharged until two weeks have elapsed."

By following this procedure in a group of thirty children (twenty-two of whom received injections of 40 cc. of whole blood, eight others having had measles), only one case of modified measles developed, and an active service was maintained. Injections were not all given on the same day, but varied from one to five days following exposure. During the period of quarantine, there were eighteen new admissions to the ward, in none of which measles developed. The isolated case of measles that did develop was of a very mild character with only slight fever, very little rash and a few Koplik spots. There were no catarrhal symptoms.

Waddell, Jr., University, Va.

Vaccination for Smallpox: The Three-Point Chisel Method. George M. Stevens, California & West. Med. **39**:243 (Oct.) 1933.

A method of vaccination using three points of inoculation in triangular arrangement is presented, the arguments in favor of its use, the technic and the results of its employment in a large series of cases being given.

Marshall, San Francisco.

A Study of Over 1,500 Deaths from Measles. Health News **10**:17 (Jan. 30) 1933.

Data on 1,529 cases of measles occurring over a period of ten years were collected in an effort to show the importance of certain predisposing factors, such as age, social and economic conditions, complications, medical and nursing care, previous physical condition and concurrent respiratory infections in the community and family.

The mortality among the poor was more than twice that among those in better circumstances; this was especially true of persons in the first two years of life

(67 per cent as compared with 47 per cent). Among persons over 5 years old there were more than twice as many deaths in those in good circumstances as in those who were poor.

Bronchopneumonia was present in 89 per cent of the patients who were poor and 79 per cent of those in better circumstances. Sixty-eight fatal cases had no complications. In 689 of 1,425 cases, or 48 per cent, the infection was traceable to another case in the family. These cases could apparently have been prevented if a physician had been called early and preventive measures instituted.

AIKMAN, Rochester, N. Y.

A STUDY OF VARIATION IN HEMOLYTIC STREPTOCOCCI FROM SCARLET FEVER AND ERYSIPELAS. SOPHIE SPICER, J. Bact. **26**:505 (Nov.) 1933.

Spicer states that the investigation is concerned with the morphologic, cultural, biochemical and immunologic phases in the dissociative processes, both spontaneous and induced, of seven strains of hemolytic streptococci from patients with scarlet fever and erysipelas. Of the seven strains under study, four (two of scarlet fever and two of erysipelas) yielded spontaneous dissociation, while from the remaining three strains (two of scarlet fever and one of erysipelas) variants were obtained by induced dissociation.

The only phase of the study that had reached completion at the time of the publication of the paper was that of the determination of antigenic changes taking place as a result of variation. It was found that a change in the form of colony, though it is to the extreme rough form, is not always accompanied by a great change in the antigenic properties of the organism. On the other hand, a slight change in the form of colony may be accompanied by profound antigenic changes. Examples of each extreme were found in two strains, one of erysipelas and one of scarlet fever. In the first instance the change in the colony was from the smooth to the rough form (with the intermediate ringed). Antigenically the strain seemed to have undergone no change. In the second case, the change in the form of the colony was so slight that it could have been easily overlooked by an untrained eye or by one not "variation conscious." Serologically, however, the change was profound, as evidenced by the loss of an antigenic fraction of the original strain and the gain of a new antigenic relationship to a different strain.

STOESSER, Minneapolis.

NEUTRALIZATION OF THE SCHICK REACTION BY HUMAN BLOOD. H. E. THELANDER, J. Pediat. **4**:75 (Jan.) 1934.

In many cases, a child who had given a positive reaction to the Schick test was found to give a negative reaction after an intramuscular or an intravenous injection of blood. In most of these instances, however, the blood of the child was reported nonimmune according to the Kellogg test (antitoxin content of the blood). It is significant that in some instances as little as 4 cc. of blood rendered the Schick reaction negative but did not supply sufficient antitoxin to the blood stream to neutralize the toxin by the Kellogg method. The studies along this line are being continued.

LEMASTER, Evanston, Ill.

THE TREATMENT OF RHEUMATIC FEVER. W. W. HERRICK, New York State J. Med. **33**:131 (Feb. 1) 1933.

The usual directions for treatment are given, and special methods of treatment are discussed. Cinchoninic acid compounds (cinchophen and neocinchophen) must be used with great care because of the danger of poisoning (icterus, followed by necrosis of the liver). Their use will probably be abandoned. Nonspecific proteins must be used with great care and are not unreservedly advised. The same can be said of streptococcus antiserum or streptococcus vaccines.

Intravenous vaccination may do harm and is still on trial. Removal of foci of infection during acute attacks is dangerous. Blood cultures have become positive, and the whole picture has been made worse by such operations. Complete rest should be continued until "all evidences of cardiac enlargement have disappeared," even up to two years. Removal to Florida, southwest America, Bermuda, Cuba or Porto Rico is suggested.

AIKMAN, Rochester, N. Y.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES—NOVEMBER 5 TO DECEMBER 2, 1933, Pub. Health Rep. **48**:1513 (Dec. 22) 1933.

A further decline in the incidence of poliomyelitis continued through November. The incidence of influenza was only about 18 per cent of that reported for the corresponding period last year. The number of cases of diphtheria was slightly lower in comparison with that of the previous four week period, possibly indicating that the peak for the year was passed. While the incidence of measles and scarlet fever was the highest for this period during the past five years the incidence of meningococcic meningitis was the lowest. Smallpox and typhoid fever continued to be reported at low levels. Deaths from all causes in large cities numbered 11.2 per thousand of population.

LEMASTER, Evanston, Ill.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, DECEMBER 3-30, 1933, Pub. Health Rep. **49**:77 (Jan. 19) 1934.

Reports indicated an increase in measles slightly above the seasonal expectancy. Since February 1932 the incidence of influenza has been low. Except for the South Atlantic and South Central areas, the incidence of diphtheria showed the usual seasonal decrease. The number of cases of meningococcic meningitis was reported to be considerably below the level of that for the preceding five years. For smallpox, the number of cases (515) was approximately the same as that for the corresponding period of 1932. For three consecutive four week periods the incidence of typhoid fever was higher than in 1932. For the country as a whole, scarlet fever maintained a satisfactorily low level throughout the year. All sections of the country reported the usual seasonal decline in poliomyelitis, but the incidence was still considerably above the level of 1932 and also above that of 1929. The average mortality rate from all causes in large cities was 11.2 per thousand of population.

LEMASTER, Evanston, Ill.

DIPHTHERIA-LIKE ORGANISMS FROM NASOPHARYNX. M. M. BARRATT, J. Path. & Bact. **36**:369, 1933.

A group of aberrant diphtheria-like organisms have been described which, while resembling Corynebacterium diphtheriae, differ from it in certain cultural characters, and most notably in their capacity to liquefy gelatin. The lesions produced in guinea-pigs by intradermal injection of the organisms are more papular and pustular than those following injection of typical C. diphtheriae. Diphtheria antitoxin does not prevent these cutaneous lesions and even in large doses does not save the life of the animal if more than one or two mimimal lethal does are given subcutaneously or, with some strains, even if only one is given. Toxic filtrates produce lesions of the skin which do not resemble those of C. diphtheriae. Diphtheria antitoxin, unless given in larger doses than from 80 to 100 units to one minimum lethal dose of toxin, does not protect the animal from death. The aberrant strains differ further from C. diphtheriae in being pathogenic for rats by intraperitoneal inoculation. Whenever the characters of the aberrant strains differ culturally or biologically from those of C. diphtheriae, they approach, if not completely, those of C. pseudotuberculosis-ovis (bacillus of Preisz-Nocard). Although evidence of the association of the particular strains studied with severe cases of clinical diphtheria is lacking, the occurrence in the human nasopharynx of diphtheria-

like organisms, the pathogenic effects of which in the guinea-pig are not prevented by diphtheria antitoxin, has been established. Therefore, the possibility that strains of this type play a part in the causation of cases which do not respond favorably to antitoxin cannot be altogether ignored.

AUTHOR'S SUMMARY [ARCH. PATH.].

CONTROL OF SCARLET FEVER BY ACTIVE IMMUNIZATION. J. STEVEN FAULDS, J. Hyg. **33**:353 (Aug.) 1933.

From 1928 to 1931, the Dick test was carried out on 393 adults (nurses). A 1:1,000 dilution of the toxin was found most suitable. The subjects who gave negative reactions were subsequently retested at intervals of from three to six months. Their reactions remained negative, and none of them contracted scarlet fever. Positive reactions were found in 23 per cent; these subjects were given serum. The initial dose was 500 skin test doses, which was doubled weekly until a dose of 20,000 was reached. There was little reaction, and no subject had a temperature over 99 F. Five per cent of those whose reactions became negative under treatment later gave positive reactions, but none contracted scarlet fever. Twelve and five-tenths per cent of those who showed positive reactions continued to give such reactions, even after efficient treatment. In this group as compared with a former group the incidence of scarlet fever was cut more than half.

Persons reared in the country and those reared in the city gave negative reactions to the Dick test in about equal numbers. Those with recurring sore throats had increased immunity against hemolytic streptococci. Two hundred children on whom the Dick test was carried out were subsequently tonsillectomized, and cultures were made from the deep tonsil substance. Such studies indicate that streptococcic infections of the throat, even when not of the scarlet fever group, may cause negative Dick reactions. Repeated slight infections of the throat by hemolytic streptococci are probably responsible for the fact that from 90 to 100 per cent of the children 1 year of age gave positive reactions while only 30 per cent of those aged 8 years reacted positively.

JANNEY, Wauwatosa, Wis.

THE STATISTICS OF ERYSIPELAS IN ENGLAND AND WALES. W. T. RUSSELL, J. Hyg. **33**:421 (Aug.) 1933.

This is a review of the history and statistics of erysipelas in England since 1871. The mortality rate is 34 per million of those in the first five years of life and 2 per million of those from 5 to 10 years of age (the lowest rate). It gradually increases to about 18 per million of young adults and to 153 per million of the aged, the average death rate being 6 per cent. The more crowded the living conditions the higher are the incidence and the mortality. The seasonal incidence runs almost parallel with that for scarlet fever and that for puerperal fever, being highest in the late winter and early spring, with a gradual shifting of the maximum from winter to spring as the years go by.

JANNEY, Wauwatosa, Wis.

BRUCELLA INFECTIONS, WITH PARTICULAR REFERENCE TO UNDULANT FEVER IN THIS COUNTRY [SCOTLAND]. T. J. MACKIE, Tr. Edinburgh Med.-Chir. Soc., 1933, p. 137; in Edinburgh M. J., August 1933.

Mackie, a bacteriologist, is interested in the etiology of undulant fever, its prevalence in Scotland, its importance as a public health problem, its sources and the modes of its transmission. The incidence is increasing from year to year, and there is a possibility that it may become a serious problem.

It has been shown that in Scotland veterinarians and slaughterers who come in contact with infected animals may become infected without showing signs of the disease. A laboratory colleague who had worked with infective material and

with cultures of Alcaligenes abortus for nearly a year found that his own agglutination titer was significant, namely, 1:320. Two students in veterinary clinical practice had a similar serum reaction, though with no ill health. All data show that manifest and latent infection is sufficiently prevalent to demand public attention as a health problem.

In Scotland the disease occurs most frequently in persons from 21 to 30 years old; males are affected more often than females. The author does not give the percentages of children affected; however, he mentions the fact that children and calves are more resistant to infection than are adults. It is possible that latent infection may be followed by immunity in children, if the source has been infected milk.

The strains of Alcaligenes which the author has isolated from milk in Scotland have all been of the bovine type. The organism is of low virulence in the average person, though individual resistance and doses are factors which have to do with determining infection and results. Raw milk and cream are probably the sources of A. abortus in Scotland. The mortality is low. Undulant fever is not a serious menace, but it should be combated so as to safeguard the milk supply.

NEFF, Kansas City, Mo.

EARLY DIAGNOSIS OF THE MENINGEAL TYPE OF POLIOMYELITIS. M. JACCOTTET, Arch. de méd. d. enf. **36**:528 (Sept.) 1933.

The extreme difficulty in differentiating between frank meningitis and poliomyelitis with meningeal symptoms dominating the onset is discussed by the writer in reporting a case of the latter infection in a girl, aged 7, and one in a boy, aged 5.

The cerebral form of poliomyelitis was first described in 1905 by Wickman; few cases have been reported up to the present epidemic in Europe and America, when a relatively large number of these invasions were found. It would appear that the disease is undergoing an evolution, with the virus manifesting an increasing tendency to attack the axis of the nervous system at a higher point. Duhem avers that in no infectious disease do the meninges become involved so frequently as in poliomyelitis; he maintains that there is no clinical symptom of meningitis which cannot be found in poliomyelitis. In the examination of the spinal fluid, however, there may be a means of separating the infections; in infantile paralysis, the average number of cells is low, usually between 100 and 300, whereas in meningitis the average is from 1,600 to 2,800. There is also in the former a distinct lymphocytosis, with normal chloride and dextrose content; the latter elements are diminished in meningitis.

AMESSE, Denver.

PHOSPHORUS METABOLISM DURING THE COURSE OF DIPHTHERITIC ANGINA. E. LESNÉ, ZIZINE and S. B. BRISKAS, Bull. Soc. de pédiat. de Paris **30**:113 (Feb. 16) 1932.

Seventy-three cases of diphtheria were studied. Repeated determinations of the inorganic phosphorus content of the blood were made during the course of the disease. It was demonstrated that the inorganic phosphorus of the blood was diminished in patients with malignant diphtheria, while the nitrogen was high and the cholesterol low.

BENJAMIN, Montreal, Canada.

ANTIDIPHTHERITIC SERUM THERAPY IN THE PEDIATRIC CLINIC AT FLORENCE IN THE YEARS FROM 1894 TO 1932. C. COMBA, Riv. di clin. pediat. **31**:1025 (Sept.) 1933.

Some recent articles in the Italian medical literature, raising doubt as to the therapeutic value of diphtheritic antitoxin, have led Comba to make a review of his cases. In 1873, Morelli-Nesti reported the cases of diphtheria in Florence

during the second half of the year 1871; this was before serum therapy had been discovered.

Age, Years	Number of Cases	Percentage of Deaths
0- 1	41	73
1- 2	112	62
2- 4	295	61
4- 7	348	44
7-10	139	32
over 10	359	6

Data for a similar table have been gathered by Comba, on 5,551 patients with diphtheria treated with antitoxin and followed up in the pediatric clinic at Florence. This table reports the cases seen there from the year 1894, when diphtheria therapy was first acknowledged, until 1932.

Age, Years	Number of Cases	Percentage of Deaths
0- 1	317	34
1- 2	1,008	29
2- 4	1,887	15
4- 7	1,540	9
7-10	526	9
over 10	273	4

Among the 5,551 cases were included 195 cases (with 77 deaths) of diphtheria secondary to measles; 168 (with 71 deaths) of the patients had involvement of the larynx.

The author believes that the experience in the pediatric clinic at Florence leaves no doubt that serum therapy in diphtheria is efficacious and that the percentage of deaths and that of complications, such as paralysis, nephritis and bronchopneumonia, rapidly increase with the passing of time from the onset of the disease until the antitoxin is given.

HIGGINS, Boston.

MORBIDITY AND MORTALITY IN DIPHTHERIA, ESPECIALLY AS INFLUENCED BY THE INDIVIDUAL PATIENT. D. MOGGI, Riv. di clin. pediat. **31**:1055 (Sept.) 1933.

The author has studied the data regarding the 181 cases of malignant diphtheria seen in the pediatric clinic of Florence between 1894 and 1932. Malignant diphtheria refers not to the cases with laryngeal and bronchopneumonic symptoms, but to those showing the presence of: (1) extensive pseudomembranous exudate on the tonsils, pharynx, palate, nose and other parts; (2) noticeably fetid breath from tissue necrosis; (3) marked cervical adenitis (bull neck); (4) signs of renal damage; (5) signs of poor peripheral circulation (pallor and weak, irregular pulse); (6) cutaneous hemorrhage, and (7) vomiting.

One hundred and eleven of the 181 patients died, although all received antitoxin. Diphtheritic paralysis developed in 42 of the 181 patients. Of those receiving antitoxin on the first day of the disease, 37.5 per cent died, on the second day 50 per cent, on the third day 59 per cent, on the fourth day 61 per cent and on the fifth day or later 74 per cent. Malignant cases comprised from 2.5 to 5 per cent of the total cases of diphtheria seen in the clinic. Moggi believes that the occurrence of the malignant case depends (1) on the virulence or toxicity of the strain of diphtheria bacilli, (2) on the treatment of the patient and (3) on individual susceptibility. Some persons may have a particular, and possibly hereditary, susceptibility to diphtheria toxin. Others do not produce antitoxin in appreciable amounts. The value of prophylactic immunization to diphtheria is stressed.

HIGGINS, Boston.

A CASE OF ACUTE GENERALIZED TETANUS CURED BY INTENSIVE SEROTHERAPY. CAMNER and MARIE CAMNER, Bull. Soc. de pédiat. de Iasi **3**: 94 (Oct. 31) 1932.

Tetanus developed in a girl aged 11 years seven days after she had stepped on a nail. The treatment consisted of chloral hydrate, solution of dextrose and massive doses of antitetanic serum. From 100 to 125 cc. of the serum was

given daily for twenty-seven days. A total of 1,835 cc. of serum (708,000 units) was given by the following routes: 635 cc. intramuscularly, 1,040 cc. intraperitoneally, 125 cc. subcutaneously, 15 cc. intraspinally and 20 cc. intravenously. Recovery was uneventful except for serum sickness. The authors emphasize the necessity of large doses of serum and the value of intraperitoneal administration.

LEMASTER, Evanston, Ill.

ROSEOLA INFANTUM. ALVIMAR DE CARVELHO, Arch. de pediat., Rio de Janeiro **5**:333 (July) 1933.

In a child the condition ran a typical course with slight fever, a macular eruption and lymphocytosis. The treatment was entirely symptomatic.

SANFORD, Chicago.

SUPPURATING PNEUMONIA AND ABSCESS OF THE LUNG IN EARLY INFANCY. PEDRO DE ELIZALDE and PASCUAL R. CERVINI, Rev. med., Buenos Aires **7**:1, 1933.

Six cases of pneumonia in infants are given in detail, including roentgenograms and photomicrographs of the pathologic process in the cells involved in suppurations following the pneumonia. Four cases of abscess of the lung detailed with roentgenograms are given. In all cases of prolonged pneumonia, tuberculosis must first be thought of and then abscess of the lung. Roentgenograms are of value, but the actual aspiration of pus is the only true basis for diagnosis. The prognosis in all cases in early infancy is bad.

SANFORD, Chicago.

THE DIAGNOSIS AND TREATMENT OF PYURIAS OF INFANCY. C. NOEGGERATH, Rev. med., Buenos Aires **7**:22, 1933.

The author describes an apparatus he uses to hold the child in the proper position for taking simple roentgenograms or views after the injection of contrasting mediums. The literature is reviewed as to the dietetic treatment of this condition.

SANFORD, Chicago.

OTITIS MEDIA IN SCARLET FEVER. F. RADE, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **24**:126 (May) 1933.

Rade presents a statistical study of the otitis media of scarlet fever from a survey of 2,835 cases of scarlet fever. The incidence of scarlet fever was greatest in March and October, whereas most of the cases of otitis occurred in February, April and June. Years of large epidemics were marked by a high percentage of otitis. The percentage of cases of otitis ran parallel not with the mortality but with the morbidity. In 12.64 per cent of all patients with scarlet fever otitis developed; in 31.5 per cent of the cases the otitis was bilateral. Otitis developed in 28.64 per cent of the children between 2 and 3 years of age, but in only 3.12 per cent of the children between the ages of 12 and 14. In most cases the otitis appeared early in the course of the scarlet fever. In 23.6 per cent of the cases it appeared during the first three days, and in 17.2 per cent of the cases during the fourth week as a second manifestation of the disease. Only a small number of cases of otitis developed between these two periods, and these usually resulted not from the scarlet fever itself but from its complications. The mastoiditis occurred in patients who no longer had any complications except otitis and in whom the otitis had developed at the beginning of the disease. Of the 41 patients who died of scarlet fever, 8 had otitis, but only 1 died from the sequelae of the otitis.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

GRIP AND PARODONTITIS. KAREL BREUER, Zubni lék. **32**:149 (June) 1932.

Gingivitis and parodontitis are not uncommon as sequelae of grip, and stomatitis of the ulcerative or even of the Vincent type may result. The author reports a case of severe gingivitis and parodontitis which involved all of the teeth to such a degree that they were loose in their sockets. The etiologic factor was an infection due to grip. Syphilis, diabetes, metabolic disturbances and other diseases were carefully ruled out. Fixation with wire and active treatment with a lavage of oxygen resulted in recovery without loss of the teeth. STULIK, Chicago.

Chronic Infections

LATE CONGENITAL SYPHILIS. A STUDY OF THE RESULTS OF TREATMENT IN TWO HUNDRED AND SIXTY-SEVEN PATIENTS. FRANK R. SMITH JR., Bull. Johns Hopkins Hosp. **53**:231 (Nov.) 1933.

This is an analysis of data on 462 patients over 13 years of age with late congenital syphilis, and of the results of treatment in 267 of the patients who were observed for more than two years.

In none of the cases was the mother treated for syphilis during pregnancy, and in 89.7 per cent of the cases a history of syphilis in infancy was absent. Two and six tenths per cent of the patients had received treatment judged to be inadequate. Smith concludes from this that in late congenital, as in late acquired, syphilis, lesions tend to appear particularly in children in whom the infantile infection ran a mild and usually unrecognized course; secondly, that treatment given early for congenital syphilis probably prevents the subsequent development of lesions or stigmas in a high proportion of patients.

The plan of treatment was to give old arsphenamine (606)), alternating with a heavy metal. Up to 1925, mercury was given by inunction; after that date, bismuth salicylate was used intramuscularly. These drugs were given by the continuous method, in alternating courses, arsphenamine in from six to eight weekly injections, the heavy metal in from six to twelve weekly injections. Rest periods were given, and an attempt was made to continue the treatment for two years. The table shows the relationship of the amount of treatment to the clinical outcome.

Treatment	Number of Patients	Number with Satisfactory Clinical Outcome
Inadequate	122	102 (83.6%)
Moderate	50	36 (72.0%)
Adequate	95	73 (76.8%)

In discussing the results of treatment, Smith establishes arbitrarily three categories, in which the classification is by time rather than by dosage. These are: (1) results of inadequate therapy, less than thirty weeks of treatment, which means fifteen or less doses of an arsphenamine, calculated for age and weight; (2) results of moderate therapy, between thirty and fifty weeks of treatment, with an equal proportion of doses of arsphenamine and one of the heavy metal compounds; (3) results of adequate therapy, fifty or more weeks of treatment. It was surprising that the clinical outcome was equally satisfactory regardless of the amount of treatment given.

Smith also notes that in late congenital syphilis the serum reaction is frequently Wassermann-fast and that there is little relationship between the amount of treatment and the reversal of the Wassermann reaction. The fact that the serum reaction is Wassermann-fast is not of unfavorable prognostic import from the standpoint of the ultimate clinical outcome. LYTTLE, New York.

TUBERCULOSIS IN CHILDREN. LEE FOREST HILL, J. Pediat. **3**:641 (Oct.) 1933.

The article is a critical discussion of the contributions to this subject published during the past year. The main topics include terminology and classification, resolving lesions, immunity, prognosis, treatment and the finding of cases.

LEMASTER, Evanston, Ill.

TWO CASES OF DEMENTIA PARALYTICA, INFANTILE AND JUVENILE. L. BALLIF and I. LUNERVSKY, Bull. Soc. de pédiat. de Iasi **3**:105 (Oct. 31) 1932.

Two cases of dementia paralytica are reported, one occurring in a girl aged 9 years, the other, in a boy aged 16 years. Both children showed mental changes, unequal pupils, exaggerated reflexes, globulin in the spinal fluid and a positive Wassermann reaction.

LEMASTER, Evanston, Ill.

INFECTIOUS DISEASES: POLIOMYELITIS. P. NÉLIS and J. GEENS, Rev. belge d. sc. méd. **5**:317 (April) 1933.

E. Schultz reported in the *Strasbourg médical* for Aug. 25, 1931, a total of four hundred and five cases occurring in the epidemic of acute poliomyelitis in the lower Rhine district from June to October, 1930. Seventy-nine per cent of the patients were children less than 6 years; 16 per cent were from 6 to 13 years of age; 5 per cent were adolescents up to 21 years of age. The total mortality was 10 per cent; 7.5 per cent of those who died were in the preschool group, 16 per cent were at the school age, and 20 per cent were among the adolescents. The epidemic prevailed along the banks of the Rhine and of some of its confluents. As the contagion extended the virus seemed to establish a regional immunity, no new outbreaks occurring where it had once passed. It appears to have had a predilection for localities on the river bank, and to have selected communities in shaded situations in the forest, avoiding those on high ground. The breaking out and progressive development of the epidemic were preceded by ten or fifteen days of excessive heat. The maximum morbidity coincided with the lowest level of subterranean water supply. Whenever the facts could be learned, they indicated the possibility of transmission of the virus by human contact. In no case could exclusive proof of propagation through food or drink be obtained.

A. Laquerrière, D. Léonard and Émile Ménard presented in the *Presse médicale* of Aug. 20, 1932, certain clinical considerations respecting the epidemic of infantile paralysis in Montreal in 1931, affecting six or seven hundred children in a population of more than a million inhabitants. It developed on the bank of the St. Lawrence River in a season of exceptional dryness when the subterranean water level was so low that many wells were dry. This epidemic ceased immediately with the coming of the first frost, which unfortunately was unusually late. Personal contagion was not apparent in most instances. The authors consider it unlikely that a child will contract infantile paralysis because its brother has the disease; they think rather that some unknown external factor affects both children at the same time. Furthermore, there was a multitude of minor febrile states which must be rated as very attenuated forms of the disease. Painful manifestations were frequent, but no relation between the pain and the severity of the paralysis was traceable. Two instances of lasting disturbances of sensation were without serious sequelae; others were free from pain, yet had marked sequelae.

VINTON, Brooklyn.

Internal Diseases

NIEMANN-PICK'S DISEASE AND OTHER FORMS OF SO-CALLED XANTHOMATOSIS. LUDWIG PICK, Am. J. M. Sc. **185**:601 (May) 1933.

This article gives a concise comprehensive comparison of Niemann-Pick's disease and other forms of xanthomatosis, namely, Hand-Schüller-Christian's disease and Tay-Sachs' disease. Niemann correlated his observations on this condition with Gaucher's disease, maintaining that the primary differentiation from Gaucher's disease consisted in the early age and the rapid, malignant course.

Niemann-Pick's disease (essential internal xanthomatosis) is a congenital constitutional and familial disease affecting predominantly the female and showing a predilection for the Jewish race. Constant clinical manifestations are enlargement of the liver and the spleen in the first months of life, rapid increase in the size of the abdomen, pale and yellowish-brown discolorations of the skin of the

parts exposed to light, slight ascites, edema and bronchitis. The superficial lymph nodes are moderately enlarged. The urine remains normal. There are moderate anemia, occasionally leukocytosis in the late stages and sometimes leukopenia. The presence of large vacuoles in many of the lymphocytes and polymorphonuclear leukocytes is noteworthy. The blood platelets are normal, the Wassermann test is usually negative and the cholesterol content of the blood is markedly elevated, although at times it is approximately normal. As the disease progresses, an extraordinarily large abdomen develops, owing to the enlargement of the liver and spleen, which become smooth and hard. Simultaneously there is general emaciation.

The differential diagnosis embodies Hanot's cirrhosis, Jaksch-Hayem's anemia, acholuric jaundice and syphilis. Complete diagnostic certainty is afforded by demonstrating the characteristic cells (the large vacuoles spoken of previously) filled with lipoid. This may be shown by puncturing the spleen or the bone marrow. A more complete description of these cells is given.

Following splenectomy there may be transitory improvement, but the malignant course is not prevented. Death may occur within a few months or as late as the second year. The observations at necropsy and photographs of the smears of cells from Niemann-Pick's disease are given.

The author dismisses the objections that have been used against the classification of the generalized essential xanthomatoses or lipoidoses with the three diseases named by stating that all natural phenomena necessarily show such transitions.

HENSKE, Omaha.

CERVICOVAGINITIS OF GONOCOCCAL ORIGIN IN CHILDREN. W. M. BRUNET, D. M. TOLLE, S. A. SCUDDER and A. R. MEDCALF, Hosp. Social Serv. Mag., supp. 1, March 1933.

An intensive investigation of gonococcic vaginitis in children was conducted as a project of the Bellevue-Yorkville Health Demonstration of New York City. The report is based on the observation of 322 young children referred because of vaginitis. The study demonstrates exceptionally close cooperation between the persons working on the medical, bacteriologic and sociologic aspects of the problem. Part I consists of the clinical reports of the physicians treating the patients. Endoscopic examinations showed that the cervix was involved in about 80 per cent of the cases. The course of the disease and the results of various methods of treatment are discussed. The bacteriologic report in part II is especially thorough and complete. The various staining methods, cultures, provocative tests and other tests are considered.

Part III contains a report of the social service aspects of the investigation, with methods of procedure, case histories and presentation of the problems encountered.

This report summarizes concisely the difficulties met in the management of gonococcic vaginitis and contains constructive and practical suggestions of definite value to persons who have the responsibility for dealing with this condition.

LEMASTER, Evanston, Ill.

THE CLINICAL IDENTITY OF VISCEROPTOSIS (GLENARD'S DISEASE) AND RECESSIVE STATUS LYMPHATICUS. HARRIS H. HOUGHTON, M. J. & Rec. **137**:184 (March 1) 1933.

Evidence is given to indicate that the clinical condition of visceroptosis and the pathologic syndrome of recessive status lymphaticus are usually identical from a clinical point of view, and that differentiation between the two is impossible. The term vagotonia emphasizes the part played by imbalance of the autonomic nervous system and refers to the same complex. Both the conditions described should be classed as chromaffin deficiency diseases. Coloptosis, megacolon, mobile cecum and undescended colon, with the formation of kinks or adhesions, are enteric anomalies of like character which are probably pathognomonic of lymphatism after puberty.

WILLIAMSON, New Orleans.

VALUE OF SANTONIN IN INFANTILE ASCARIASIS. M. P. SCHIKHOBALOVA and E. W. SOKOLOVA, Rev. franç. de pédiat. **8**:610, 1932.

The authors estimate that the feces of 40 per cent of the infant population of Moscow contain the eggs of Ascaris. In the treatment of these children the authors obtained the best results with santonin, 0.05 Gm. being given to children of from 8 to 10 years of age, and 0.06 Gm. to children of 11 and 12 years. The doses are given at intervals of nine, ten and eleven hours. On the third day the patients are given a saline purge. By this method 86 per cent of the children were sterilized. The organisms are expelled as late as the sixth day, not only from adults but also from the young. The authors believe that santonin is a remedy par excellence.

SANFORD, Chicago.

BLOOD TRANSFUSION IN THE TREATMENT OF BRONCHOPNEUMONIA. G. PHÉLIZOT and B. TASSOVATZ, Rev. franç. de pédiat. **8**:695, 1932.

The authors injected 20 cc. of blood per thousand grams of body weight into infants up to 8 months of age, and 15 cc. into older children. The actual amount varied from 50 to 150 cc. The authors used a 10 per cent citrate solution to 100 cc. of blood and made injections into the longitudinal sinus if possible. In twenty-five severe cases of bronchopneumonia, four patients received transfusions while moribund; they died. Of the remaining twenty-one, seventeen recovered, and four died after amelioration of the symptoms. Phélizot and Tassovatz consider that transfusion is of remarkable therapeutic value in bronchopneumonia.

SANFORD, Chicago.

VAQUEZ' DISEASE TREATED WITH SUCCESS BY ONION JUICE. L. BOISSONNAS, Rev. franç. de pédiat. **8**:745, 1932.

A girl, aged 15 years, had red cells numbering 8,400,000, with 90 per cent hemoglobin. She was given 150 Gm. of onion juice, and in ten months the red cells had fallen to 4,600,000, with 76 per cent hemoglobin. This treatment was based on the experiment of Gruhzit, who obtained severe anemia in a dog by giving 15 Gm. of fresh onion per kilogram of body weight. The decrease in red cells is evidently due to hemolysis.

SANFORD, Chicago.

ACUTE ILIAC ADENITIS IN CHILDREN. R. M. DEL CAMPO and C. M. BARBEROUSSE, Arch. de pediat. d. Uruguay **4**:43 (Feb.) 1933.

The authors report ten cases of this disorder. Radiating pain and limitation of motion of the lower extremities are prominent symptoms. The glands practically always suppurate. In the differential diagnosis, appendicitis must always be ruled out. Only one of the cases terminated fatally.

SCHLUTZ, Chicago.

A CASE OF SOMOPSYCHOGENITAL PRECOCITY IN A 7½ YEAR OLD GIRL. F. FASSBENDER, Ztschr. f. Kinderh. **54**:642, 1933.

The author describes a case of macrosomia, precocious development and beginning sexual prematurity in a girl of 7½ years. The cause of this abnormality was traced to a tumor (possibly a teratoma), which was diagnosed roentgenologically. A good review of the literature is included.

SHELLING, Baltimore.

ABNORMAL ENLARGEMENT OF THE LIVER IN THE COURSE OF COLITIS IN CHILDREN. P. BAUMRITTER and H. HIRSZFELDOWA, Pediatria polska **12**:117, 1932.

In the course of many cases of colitis in children in the past few years, a peculiar clinical syndrome has occurred, although very rarely. It appears in children between 1 and 2 years of age and is characterized by prolonged diarrhea, violent

vomiting, enlargement of the liver about 4 fingerbreadths below the costal margin, swelling of the eyelids and the extremities and enlargement of the lymph glands. The condition lasts for several months. The authors report four cases; in two the patients died and in two they recovered. In all cases the Widal, Wassermann and Pirquet tests were negative.

KRUPINSKI, Chicago.

Nervous Diseases

A STUDY OF THE EYE FINDINGS IN A GROUP OF EPILEPTICS WITH REFERENCE TO THE MECHANICAL THEORY OF EPILEPSY. HARRY COSTEFF, Am. J. Psychiat. **11**:747 (Jan.) 1932.

On the hypothesis that a long-continued increase in intracranial pressure would manifest itself in pathologic conditions within the eye, Costeff undertook to study the eyegrounds of epileptic patients to determine the frequency, constancy, persistence and significance of changes in the fundi of these patients. His group consisted of 114 epileptic persons ranging in age from 17 to 77. In 9 instances the fundus could not be visualized; of the remaining cases, normal eyegrounds were found in 46, or 47 per cent. In more than half the cases, therefore, an abnormality was found. There were 32 instances of hyperemia of the fundus, 17 of optic atrophy and 11 of choroiditis. In 45 of the 59 patients who presented ocular disease, the condition seemed permanent. The fact that so large a group exhibited an identical pathologic condition (passive hyperemia) is significant. Costeff considers the existence of passive hyperemia as evidence of increased intracranial pressure. He reasons that in the eyeground there must be an equilibrium between the venous pressure and the pressure of the surrounding fluid medium—the cerebrospinal fluid. Consequently an increase in the pressure of the latter will be met by compensatory changes in the retinal vessels. His work tends to support the hydraulic theory of the cause of epilepsy.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

EPILEPSY: XIII. AURA IN EPILEPSY; A STATISTICAL REVIEW OF ONE THOUSAND THREE HUNDRED AND FIFTY-NINE CASES. WILLIAM G. LENNOX and STANLEY COBB, Arch. Neurol. & Psychiat. **30**:374 (Aug.) 1933.

This is a careful tabulation of the aura in 1,359 noninstitutional patients with epilepsy. An aura was present in 56.2 per cent of the number reported on.

BEVERLY, Chicago.

ANENCEPHALY IN IDENTICAL TWINS. J. E. JOSEPHSON and K. B. WALLER, Canad. M. A. J. **29**:34 (July) 1933.

A case of anencephaly in each of female twins, probably identical, is described. The confinement was the ninth of a mother 29 years of age. Several children in the family showed mental or physical deficiency.

While both twins showed a gross cranial defect, one of them showed numerous internal defects such as diaphragmatic hernia and hernia of the liver in the umbilical opening. The other twin showed little deviation from normal in regard to its gross internal anatomy.

In both children the suprarenal glands were smaller than the average usually accepted, and there was an increased development in the definite zona glomerulosa and zona fasciculata.

Only the anterior lobe of the pituitary gland was found in each twin.

MOORE, Omaha.

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. HOWARD B. METTEL and Y. K. SLOCUM, J. Pediat. **3**:352 (Aug.) 1933.

Of thirty-eight patients with pseudohypertrophic muscular dystrophy treated by various methods, none showed improvement except two of three patients treated with glycine. There were wide fluctuations in the daily excretion of creatine. The authors believe that their initial results with glycine warrant further studies in its use in this disease. LEMASTER, Evanston, Ill.

EPILEPSY: THE VALUE OF ENCEPHALOGRAPHY IN THE SELECTION OF PATIENTS FOR TREATMENT BY THE KETOGENIC DIET. R. CANNON ELEY, J. Pediat. **3**: 359 (Aug.) 1933.

Twenty-nine children suffering from idiopathic epilepsy were subjected to encephalography prior to the institution of the ketogenic diet. Of twenty-one patients with normal encephalograms, nineteen responded favorably and only two unfavorably to the dietary regimen. Among the eight patients showing abnormalities in the encephalogram the condition of only one was improved by prolonged ketosis. The author believes encephalography to be an extremely valuable aid in determining the prognosis and proper treatment for epileptic patients. Other methods of treating epilepsy are briefly discussed. LEMASTER, Evanston, Ill.

ALLERGIC EPILEPSY. J. KLEIN, J. Pediat. **3**:505 (Sept.) 1933.

The relationship between allergy and certain types of idiopathic epilepsy is discussed. The author reports one case in which an 8 year old girl had a markedly allergic constitution as shown by eczema, hay fever, asthma and many positive tests of the skin. The patient also had numerous epileptic seizures. After receiving sodium thiosulphate she had no further convulsions and only two mild attacks of asthma. It is suggested that both the asthmatic and the epileptic symptoms may be due to the underlying allergic reaction.

LEMASTER, Evanston, Ill.

THE BIOLOGICAL AND SOCIAL BACKGROUND OF A TANTRUM CASE. E. C. ROWE, Ment. Hyg. **16**:610 (Oct.) 1932.

Rowe believes that in explaining temper tantrums as a form of response there is a tendency to place too much emphasis on training and too little on hereditary qualities. It is his contention that there are great individual differences in the ease with which this pattern of response is acquired, and that these differences depend on inherited characteristics. The hypothesis is illustrated by the report of the case of a girl, aged 12, who lived with her mother in an orphanage. The girl was physically well developed and free from illness, and had an intelligence quotient of 123. Eager and active, she was readily moved to tears or to outbursts of extreme anger. This cannot be accounted for on the assumption that the mother "spoiled" the child by catering to her whims, for the fact is that the tantrums appeared at the age of 2, and that the mother ignored or punished them for several years, adopting the policy of indulgence only after sterner methods had failed. An equally intelligent, but emotionally much more stable, older brother, who had been subjected to an early training in every way similar to that of the girl is cited as evidence of the relative ineffectiveness of training as an explanation of the tantrums. An investigation of the family history showed different emotional trends in the two sides of the family. The father was good-natured and easy-going; the mother as a girl had been a sulky, pouting child, and was herself the daughter of a stern, "hot-tempered" father. It is Rowe's opinion that the boy can be described as a replica of his father, while the girl possessed the temper of her mother and maternal grandfather. The existence of significant environmental factors, however, is not denied. At the age of 6 the girl was placed in a dormitory with thirty

other children; the matron was a stern disciplinarian. The other children, intellectually inferior to the patient, lost no opportunity of taunting her, to compensate for their own feeling of inadequacy. The girl's mother had been promoted, and the older members of the orphanage force resented this advancement and treated the child accordingly. The mother was eventually placed in a position in which she was obliged to report girls for misbehavior, a situation that further stimulated mistreatment of the patient. As no mention is made of the disposition of the brother, the presumption is that he was living in a more sympathetic environment.

The author concludes by discussing the technic of the individual management of problem children of this sort. That improper training can produce the temper tantrum pattern of response is not denied, but a plea for the recognition of the hereditary factor is made.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

CEREBELLAR TUMOUR? RIGHT LOBE. REGINALD C. JEWESBURY, Proc. Roy. Soc. Med. **30**:1017 (June) 1933.

The patient was a girl of 7 years. She had suffered from headaches for one month, which were followed three weeks later by attacks of vomiting. On admission to the hospital she was drowsy, but answered questions quite rationally. She could not stand or sit up. The right disk was indefinite in outline. No nystagmus was present. The child was deaf on one side, and there was a slight facial weakness. There was marked cerebellar incoordination with hypotonia in the right arm and leg. The tendon reflexes were absent on the right side. A roentgenogram of the skull showed nothing abnormal.

WILLIAMSON, New Orleans.

ACID-BASE EQUILIBRIUM OF BLOOD IN EPILEPSY. FRANCIS LEO MCLAUGHLIN and RICHARD HENRY HURST, Quart. J. Med. **2**:419 (July) 1933.

In cases of idiopathic epilepsy the author measured the p_H, alkali reserve and lactic acid of the blood.

The results suggested that in the interval between fits: 1. Variations in alkali reserve and lactic acid are usually within normal limits, but those of p_H extend to a range slightly above normal. 2. The average lactic acid concentration is normal. The average alkali reserve and p_H values tend to be slightly above normal.

The averages of results obtained for alkali reserve and p_H during the two hour period preceding the attack show no significant difference from those of the intervening period.

Results of analyses done before, during and after seizures were as follows:

"There is a fall in alkali reserve during, and for varying periods after the fit, this fall being accounted for by the accumulation of lactic acid in the blood. Decrease in lactic acid during recovery is accompanied by increase in alkali reserve.

"The blood p_H falls during the fit, due firstly to apnoea during the tonic stage, and secondly to production of lactic acid during the clonic stage. Recovery to normal p_H is more rapid than is the case with normal individuals after exercise."

The methods used are thoroughly described. BRADFORD, Rochester, N. Y.

CONGENITAL MENINGO-EPENDYMITIS OF MENINGOCOCCIC ORIGIN. M. B. COLOMB and A. BARSKY, Arch. de méd. d. enf. **36**:467 (Aug.) 1933.

Pyocephalus in the new-born has been reported by numerous writers since the first case was described by Lequeux in 1910. The organisms commonly involved are the streptococcus and the staphylococcus and occasionally the pneumococcus, the colon bacillus and similar bacilli. Root, in 1921, observed several instances of

this infection, which he traced to the meningococcus, and the authors found, during the seven years from 1926 to 1932, inclusive, 4 further cases in new-born infants in a series of 403 at their clinic in Russia.

A case history is offered with the results of autopsy and an exhaustive discussion of the pathogenesis.

AMESSE, Denver.

PATHOLOGIC ANATOMY OF SO-CALLED EXPERIMENTAL POSTVACCINAL ENCEPHALITIS. HAROLD SCHMID, Encéphale **28**:337 (May) 1933.

This article reports experiments involving injections of smallpox vaccine both by the direct parietal route and through the orbit. Descriptions of the changes in ganglion and glia cells are given. However, conclusions are difficult to draw because, just as in all such experimental work, it is not possible to limit the zones of action of the invading material. Both meninges and brain proper will be involved in varying degrees—whatever the location of the injection. To account for limited actions the author assumes some kind of "hemato-encephalic" barrier, which can operate in a selectively defensive manner. At times this mechanism can "detoxicate" the virus or at least render it incapable of affecting the brain.

ANDERSON, Los Angeles. [ARCH. NEUROL. & PSYCHIAT.]

THE DEVELOPMENTAL PROFILE IN THE PRACTICE OF CHILD NEUROPSYCHIATRY. GEORGES D'HENCQUEVILLE, Hyg. ment. **28**:101 (March) 1933.

The entire number of the journal is given over to presenting a technic applicable to the study of child neuropsychiatric problems. It is designed to be rapid and to permit of interpretation at the time of study. It presents a series of tests of various functions, motor, sensory, verbal, etc., which can be put into graphic form against a more or less accepted normal. It is of greater prognostic than diagnostic value.

ANDERSON, Los Angeles. [ARCH. NEUROL. & PSYCHIAT.]

PSYCHOTHERAPY FOR INSTITUTIONAL BABIES. D. MORITZ, Nourrisson **21**:209 (July) 1933.

Others have emphasized the importance of psychic appeal in the care of infants, and the author cites four cases in which this factor alone seemed responsible for a marked increase in weight after a stationary period. The ages of the babies varied from 7 to 10 months. They were suffering from malnutrition and exudative diathesis.

MCCLELLAND, Cleveland.

FAMILIAL INCIDENCE OF A PECULIAR TYPE OF HEREDITARY DISEASE. A. POPOW, Rev. neurol. **2**:447, 1932.

The author describes a familial disease, confined exclusively to males and characterized by weakness of the arms and legs, slight atrophy of the muscles of the hands and of the lower third of the legs, absence of deep reflexes, impaired reactions to electrical stimuli and pes cavus. It is not progressive, and the condition tends to improve with age. In childhood it resembles Friedreich's ataxia, while in adults the symptoms might be mistaken for early cases of peroneal atrophy. Except for the limitation of the disease to the male sex, this syndrome closely resembles that described by Roussy and Lévy in 1926.

SCHNEIDER, Washington, D. C. [ARCH. NEUROL. & PSYCHIAT.]

ASEPTIC OTOGENOUS SEROUS MENINGITIS: CURE. LACROIX, Rev. d'oto-neuro-opht. **10**:742 (Dec.) 1932.

The case reported is that of a young girl in whom, in the course of chronic otitis, meningitis developed. The cerebrospinal fluid contained 150 cells and 70 cg.

of albumin. No organisms were found on culture. Immediate radical mastoidectomy with wide exposure of the dura was done, and a large cholesteatoma and a perisinus abscess were revealed. A fixation abscess was produced, and rapid recovery followed. Lacroix emphasizes that the operative results are better when the fluid is clear and the cellular elements are intact, and that prompt and thorough operation is important.

DENNIS, Colorado Springs, Colo. [ARCH. NEUROL. & PSYCHIAT.]

EXPERIENCES WITH ENCEPHALOGRAPHY IN DISEASES OF THE NERVOUS SYSTEM IN CHILDREN. PIERO SIGHINOLFI and CAROLINA VIOLA, Radiol. med. **17:** 1432 (Dec.) 1930.

Ten cases of different diseases of the nervous system in which encephalography was used are described and illustrated with roentgenograms. There were no cases of immediate death, though most of the patients were in an extremely serious condition; but the method does involve considerable shock and may have the effect of making a patient worse if he is already in a serious condition. In two cases of tuberculous meningitis, in which it was hoped that the encephalography would have some therapeutic effect, the results were disappointing. There was no improvement. The ventricles did not fill in a case of tumor of the inferior vermiform process of the cerebellum or in some other cases of hydrocephalus, in which previous inflammation of the meninges had blocked the foramina of Luschka and Magendie. Paraventricular tumors were demonstrated brilliantly. The authors conclude that in the present status of ventriculography it should be used in only a few cases, at least until it has been rendered less dangerous by changes in technic, such, for example, as the decrease in the amount of gas used, proposed by Besta.

STULIK, Chicago.

PRESENCE OF ATTENUATED PNEUMOCOCCI IN THE CEREBROSPINAL FLUID OF A GIRL WITH A PNEUMOCOCCIC INFECTION WITH RESULTING CURE. A. FARIOLI, Riv. di clin. pediat. **31**:424 (April) 1933.

The author reports the case of a girl of 8 years who first became sick on Oct. 11, 1932, with slight pains in the throat and the abdomen and some rigidity of the back and the neck. On October 13 she ran an iron nail into her right foot. She then became much worse, with marked abdominal pain and a stiff neck; she was taken to the clinic, where antitetanic serum was given immediately.

A spinal puncture yielded an opalescent fluid under increased pressure, with a positive Pandy test for globulin and 0.07 Gm. of sugar per hundred cubic centimeters. There were seen red blood cells, polymorphonuclear cells, a few lymphocytes and numerous diplococci. Cultures of the spinal fluid, the blood and the pus from a gum-boil showed Pneumococcus group II. There was no discharge from the ear; the right ear drum was only slightly red, and the left normal.

Antipneumococcus serum was administered intramuscularly. The child unexpectedly began to show improvement and was discharged well on October 31. A second spinal puncture showed normal spinal fluid.

Comparison of the pneumococci obtained from the spinal fluid with those obtained from the blood and from the gum-boil showed the former to grow more slowly and to be much less virulent to a white rat. The attenuation of the organism in the spinal fluid probably explains the recovery of the patient.

HIGGINS, Boston.

THE MESENCEPHALIC SYNDROME. I. MARCIALIS, Riv. di clin. pediat. **31**:441 (April) 1933.

The author reports the case of a girl, aged 3 years, with tuberculomas of the midbrain (right and left cerebral peduncles). The patient had had malaria in August and had not been exactly well since. In November she showed irritability

and difficulty in talking. In December she could not stand alone; when held, she dragged her left leg; ptosis of the right eyelid and external strabismus were noticed. Later in the month increased weakness of the left leg and ptosis of the left eyelid appeared. There was a deviation of the mouth to the right. In February, more trouble with speech and drowsiness were added symptoms. In March, difficulty in swallowing and polyuria occurred; the patient could not sit without support. Drowsiness became more marked, and artificial means of feeding had to be used. The child died in April.

The case is interesting in showing a pure midbrain syndrome similar to that seen in epidemic encephalitis. The drowsiness and polyuria were unusually interesting symptoms.

HIGGINS, Boston.

MOTOR REACTIONS OF THE INFANT IN APPROACHING THE ERECT POSTURE. GIORGINA C. BORGIOTTI, Riv. di clin. pediat. **31**:533 (May) 1933.

The author recorded the muscular movements of normal infants aged 6, 8 and 10 months, as the ability to creep and, later, to stand, developed. The babies were placed flat on their backs; their method of rotating to get on their abdomens and then to elevate themselves is described. Photographs are given to show the three stages of movements in each age group. The status of three abnormal children—one, aged 18 months, who had rickets, another, aged 22 months, who had cerebral spasms, and a third, aged 10 years, who had chorea—is similarly described.

HIGGINS, Boston.

A CASE OF ANARTHRIA (MOTOR APHASIA): RECOVERY. JUAN C. NAVARRO and J. A. BLACK, Arch. argent. de pediat. **4**:397 (June) 1933.

The authors report a case of a practically pure form of motor aphasia in a boy of 6 years, which is interesting because of the sudden onset, the rapid recovery and the obscure etiology.

The onset was sudden in a previously healthy child, with vomiting, headache, a slight right facial palsy and incoordination of the right arm. He remained somnolent for only fourteen hours, and on the following day complete motor aphasia developed; however, the patient was able to obey commands and to take dictation. The cerebrospinal fluid was normal, and the Wassermann reaction of the blood was negative. Outside of a positive reaction to tuberculin there was no evidence of an underlying infectious process. Two days later the patient began to speak a few words, and a month later his speech was normal. There remained, however, a slight right facial atrophy.

The authors question the presence of an underlying infectious or encephalitic process in this case and suggest that the symptoms might be explained best as an acute minor focal vascular lesion.

SCHLUTZ, Chicago.

STUDIES OF THE CEREBROSPINAL FLUID: I. IN ACUTE ANTERIOR POLIOMYELITIS. LEDISLAUS VON KOSTYÁL, Arch. f. Kinderh. **100**:15 (July 18) 1933.

This study is based on 428 examinations of spinal fluid from 83 children with acute poliomyelitis. After analyzing the data, the author forms the following conclusions: 1. In poliomyelitis the cerebrospinal fluid varies greatly, not only in different persons, but also in the same person at different times. 2. There is no characteristic reaction for the spinal fluid in poliomyelitis. A diagnosis of poliomyelitis cannot be made from the spinal fluid alone, without clinical observation. 3. There is no proportion between the degree of change in the spinal fluid and the severity of the illness. 4. Improvement can be expected as long as the spinal fluid is positive. 5. It is more probable that the protein of the spinal fluid is a special and specific product of a reaction of the organism than that it is an inflammatory product.

LEMASTER, Evanston, Ill.

ROENTGEN THERAPY OF FEEBLEMINDED CHILDREN. JOHANNES JOCHIMS, Arch. f. Kinderh. **100**:27 (July 18) 1933.

In 1928, von Wieser reported favorable results following roentgen irradiation of the skulls of feebleminded children with such conditions as mongolian idiocy, microcephalia, epileptic dementia and postencephalitic conditions. Jochims treated a series of mentally deficient children by the same technic. In some cases excitable, restless children were definitely more quiet after the irradiation. In no case was any lasting beneficial effect of any kind observed.

LEMASTER, Evanston, Ill.

EPILEPSY IN CHILDHOOD. J. ZAPPERT, Ergebn. d. inn. Med. u. Kinderh. **43**:149, 1932.

The author defines epilepsy as a chronic disease which is characterized by repeated seizures in which disturbances of consciousness are typical, muscular convulsions are common and sensory, secretory and psychic phenomena occasionally occur. On account of the unfavorable prognosis, the author feels that one should be wary in making a diagnosis of epilepsy. Although there are cases of cerebral palsy that are not associated with convulsions, in cases in which convulsions occur it is sometimes almost impossible to differentiate them from true epilepsy. The author prefers the term "residual epilepsy" for that type of case.

The author discusses at length the various factors contributing to the disposition or tendency to epilepsy, especially heredity, alcoholism (this factor he considers as generally exaggerated), syphilis and internal secretions. The final impression that one gains is that Zappert does not consider these factors as important predisposing causes, but that he does attribute increased importance to cerebral injury sustained at birth as a possible forerunner of epilepsy. Although in at least a third of the cases epilepsy begins in the first ten years of life, in a sufficiently striking number the first seizures occur during infancy; this fact is of great importance because of the necessity for differentiating epilepsy from other convulsions that occur during infancy as a result of tetany, intracranial diseases, febrile disturbances and endogenous intoxications. The latter causes of convulsions in infancy are not as a rule later transformed into epilepsy. One must always bear in mind, however, that genuine epilepsy may sometimes exhibit itself in the first seizure as ordinary symptomatic convulsions during infancy. The author divides patients with epilepsy into two classes: (1) those who from infancy have attacks at frequent intervals and (2) those in whom long periods (perhaps years) elapse between the first seizure during infancy and the subsequent one. Frequently attacks will become numerous after a long quiescent period. Zappert emphasizes the frequency with which nocturnal attacks occur in epilepsy in childhood, and he even suggests the existence of a nocturnal type in which the epileptic seizures take place exclusively at night. Tonic convulsions, beginning in the face and spreading to the remainder of the body, are more common in childhood than are clonic convulsions. Decided jacksonian seizures with isolated twitchings of the limbs and retained consciousness do not belong to the childhood type of epilepsy. The occurrence of aura is not often reported in children, certainly not as often as in adults. Fainting, dizziness and nausea are the most common expressions of the aura in childhood; occasionally paresthesia of the face or of the extremities may occur. Fatigue and somnolence are regular events after an attack. Petit mal can take on various forms, such as mere attacks of winking associated with mental changes, disturbances in consciousness, rudimentary motor changes (twisting, staring and other changes), vomiting, vertigo, fainting and migraine.

The author divides epileptic children into four classes from the standpoint of intelligence. In the first group are the children with normal intelligence. The second and by far the largest group consists of children who appear quiet, obedient, simple and, in the eyes of uncritical parents, normal. However, intelligence tests

usually show them to be below normal, and after a few years there is a gradual transition into the characteristic state of dementia epileptica. The third group consists of the slightly demented children with striking psychic behavior. In the fourth class belong the imbecilic or typically idiotic children. There seems to exist no direct relationship between the mental state of the child and the frequency of seizures.

The author divides the treatment of epilepsy into three types: (1) medicinal, (2) dietetic and (3) surgical. The medicinal form of treatment he subdivides into the prebromide, the bromide and the pentobarbital periods. The dietetic form of treatment he subdivides into starvation cures and salt-poor and ketogenic diets. One gains the impression that pentobarbital given regularly in large doses over a period of many years is the author's preferred method of treatment, although he also favors somewhat a salt-poor diet, and he feels that the ketogenic diet should be given further trial.

CAPPER, Philadelphia.

THE SIGNIFICANCE OF CAPILLARY MICROSCOPY IN OLIGOPHRENIA. EMIL VON LEDERER, Monatschr. f. Kinderh. **58**:429 (Aug.) 1933.

This is a clinical discussion with four photomicrographs of capillary microscopy in oligophrenia. On the basis of fifty-five cases, the writer believes that those cases in which there has been an early injury to the germ plasm have a better prognosis than those in which the damage has come later.

Capillary microscopy offers reliable evidence as to whether or not injury to the germ plasm has been early; cases of early injury present poorly developed capillaries and cases of later injury, the reverse.

In treating the patients with mixtures of internal secretions, Lederer found that thirty of the thirty-four with the primitive capillaries were greatly improved, 88 per cent, while of thirteen patients with well developed capillaries, only four showed improvement, 38 per cent.

He believes that capillary microscopy is thus an important means of prognosis.

GERSTLEY, Chicago.

PSYCHOPATHOLOGY OF THE CHILD: A BORDERLINE SPECIALTY. CARL POTOTZKY, Ztschr. f. Kinderforsch. **41**:287 (May 17) 1933.

This article is one of three speeches delivered at a conference which was held in Germany for the purpose of establishing collaboration between psychiatrists, pediatricians and officials interested in social service. The present article is a general review of the difficulties encountered in this collaboration both in Germany and in the United States.

REICHLE, Cleveland.

ORGANIC DISEASE AS A CAUSE OF BEHAVIOR DIFFICULTIES IN A SMALL CHILD. J. IBRAHIM, Ztschr. f. Kinderforsch. **41**:298 (May 17) 1933.

Ibrahim, who is noted for his interest in the functional diseases of childhood, discusses in this article the influence of general diseases of the body on the conduct of the child. He calls attention to the fact that not only may the sense of illness give rise to an immediate behavior problem but that the compromises which the parent, nurse or physician makes during the period of acute illness often lead to permanent changes in the child's attitude toward disciplinary questions. These results are entirely independent of the type of disease and are in reality due to the apparently inconsequential attitude of the child toward its environment. The physician himself must be particularly careful to avoid causing overanxiety in the minds of the parents and also frightening the child. Furthermore, an undue length of time spent in a hospital or in any closed institution may cause serious difficulties in the training of the child. Therefore, even infants should be returned to the care of their parents or foster parents as soon as an acute illness is over.

Certain organic diseases are particularly prone to cause behavior problems. Such are intestinal infantilism, erythredema, rickets, long-standing eczema, deafness and dumbness and certain forms of disease of the bones, joints and nerves which cripple the child.

REICHLE, Cleveland.

PSYCHOPATHIC CONSTITUTION AND ORGANIC NERVE DISEASE AS A CAUSE OF BEHAVIOR PROBLEMS. FRANZ KRAMER, Ztschr. f. Kinderforsch. **41**:306 (May 17) 1933.

This is a good review of the influence of psychopathy and some of the organic diseases—encephalitis and epilepsy—on the attitude of the child toward its environment.

REICHLE, Cleveland.

CAPILLARIES OF INFANTS AND MENTALLY DEFICIENT CHILDREN. EMIL VON LEDERER, Ztschr. f. Kinderforsch. **41**:349 (May 17) 1933.

This is an investigation of the theory of Jaensch and Hoepfner, who believe that a primitive form of capillaries is found in the skin of children who are mentally deficient. The author investigated the form and character of the capillaries not only in mentally deficient children but also in infants. He found among 44 new-born 43 who had the typical form of capillary described by Hoepfner. As the infant becomes older, this form tends to develop into the adult type. He also examined 100 mentally deficient children and found that 65 per cent showed this type of infantile capillary, whereas of 100 normal children only 16 per cent showed this form.

REICHLE, Cleveland.

ATROPINE TREATMENT IN RESIDUAL SYMPTOMS OF LETHARGIC ENCEPHALITIS. R. NAKAYE, J. Pediat. (Tokyo), Aug. 20, 1933, no. 399, p. 1462.

The author treated two patients with epidemic encephalitis without parkinsonism, and found that the first patient, with altered balance of the autonomic nervous system, responded partially to massive doses of atropine, but no effect was noted in the second patient, who had changes in the cerebral cortex.

KATO, Chicago.

CLINICAL EXAMINATION OF THE SPINAL FLUID BY ULTRAVIOLET RAYS IN MENINGITIDES IN CHILDREN. S. SAITO, J. Pediat. (Tokyo), Aug. 20, 1933, no. 399, p. 1476.

When a sample of the normal cerebrospinal fluid is examined under ultraviolet rays, only a yellowish or a slightly purplish-yellow color is noted. The spinal fluid of patients with tuberculous meningitis shows a characteristic purplish-blue fluorescence under ultraviolet rays. In the spinal fluid of patients with encephalitis and myelitis, no such fluorescence is seen, in spite of definite pathologic changes in the fluid. The spinal fluids of patients with purulent meningitis or epidemic cerebrospinal fever show a beautiful fluorescence from indigo to cobalt blue. This method of examination is of value not only in diagnosis, but in prognosis of various types of meningitis. The presence of red blood corpuscles does not affect the examination.

KATO, Chicago.

FEVER OF SIX AND ONE-HALF YEARS' DURATION IN A CHILD WITH CONGENITAL MALFORMATIONS OF THE BRAIN AND SPINAL CORD AND A CONGENITAL TUMOR OF THE MEDULLA. CORNELIA DE LANGE, Acta pædiat. **14**:503 (July 12) 1933.

This is the report of the case of a boy in whom, at the age of 10 months, a complex neurologic syndrome developed, consisting in spastic and flaccid paralysis

of various muscle groups, marked sweating, protracted intermittent fever, fecal and urinary retention and muscular atrophy. Despite periods of limited improvement death ensued at the age of 7½ years.

Autopsy demonstrated congenital anomalies of the spinal cord and the brain, together with a congenital tumor of the medulla oblongata. There were bilateral hydronephrosis and a vesical concretion.

The author attempts to establish a correlation between the clinical manifestations and the anatomic findings. She comes to the conclusion that the fever was due to a disturbance of the central heat-regulating mechanism. McCUNE, New York.

Diseases of the Eye

PURULENT CONJUNCTIVITIS IN INFANTS CAUSED BY AN ATYPICAL STAPHYLOCOCCUS. J. S. PLUMER, Pennsylvania M. J. **34**:821 (Aug.) 1933.

One obtains from a review of the literature the impression that while the etiologic significance of the staphylococcus in isolated cases of ophthalmia neonatorum is generally admitted, its relative importance has been minimized and that the differential diagnosis with the gonococcus of Neisser has been afforded slight consideration. Thomas reports the isolation of metachromatic, pleomorphic Staphylococcus aureus from cases of purulent ophthalmia. As a result of the study of these cases, the author concludes:

As pointed out by others, Staphylococcus aureus may cause conjunctivitis in the new-born which in the early stages resembles clinically that caused by the gonococcus.

There is clinical and anatomic evidence that very young children are more susceptible to infection by the staphylococcus than are adults.

Smears alone, even when stained by Gram's method, cannot always be relied on. Accurate and adequate bacteriologic methods should be employed.

It is important to make a diagnosis because, owing to a notion prevailing among many of the laity and even some physicians that the majority of cases of ophthalmia neonatorum are due to the gonococcus, parents may be unjustly stigmatized and much needless mental suffering result.

By no means are all cases of ophthalmia neonatorum due to infection attending birth; the condition may develop independently from outside sources during the early days of life, as was evident in the cases reported by Thomas.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

A CONJUNCTIVAL BAND SIMULATING A PERSISTENT NICTITATING MEMBRANE. C. V. KRISHNASWAMI, Brit. J. Ophth. **17**:417 (July) 1933.

The patient presented a fold of the inferior fornix drawn up and adherent to a small area of the upper tarsal conjunctiva. It was blush pink and fan-shaped with the apex at the attachment to the upper tarsal conjunctiva and at the base at the inferior fornix, the borders being crescentic. A few blood vessels ran vertically on its surface like the ribs of a fan. Apart from its location on the outer side of the cornea, it simulated a persistent nictitating membrane. The eyeball was perfectly free underneath the band. The author has seen four other similar cases.

The article is illustrated. ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

CONGENITAL HYALINE MEMBRANES ON THE POSTERIOR SURFACE OF THE CORNEA. I. MANN, Brit. J. Ophth. **17**:449 (Aug.) 1933.

The author has examined five eyes presenting a hyaline membrane on the posterior surface of the cornea. The first case was that of a man, aged 29. Vision in the right eye with a compound myopic astigmatic correction was 6/6—, and in the left eye with a compound hyperopic astigmatic correction, 6/4—. Tension of each eye was normal, and the disks were not cupped. The right eye appeared

normal, except that the lesser circle was extremely near the margin of the pupil, and there were a few bags of vascular remnants attached to it.

In the left eye the cornea was slightly smaller than that of the right eye. The central portion of the cornea was normal. In the periphery, however, a semitransparent hyaline membrane appeared applied to the posterior surface of the cornea almost throughout its whole circumference. The inner edge of the membrane formed roughly a circle concentric with the margin of the cornea and lying at about a fourth of the distance from the limbus to the center of the cornea from it. From this inner margin, the membrane extended outward into the angle practically the whole way round, a small gap (roughly between one seventh and one eighth of the circumference) occurring in its peripheral part (though not in its inner edge) at 10 o'clock. This membrane was applied firmly to the posterior surface of the cornea round most of the circumference. In the lower part, however, it stood away from the cornea (except at its inner edge) for a short distance, forming in section a cord to the arc of the corneal nerve. It had a slightly granular texture and was imperfectly transparent. The inner edge was marked by irregular small masses of pigmented tissue (pale golden brown) similar to the pigmented tissue composing the anterior layer of the iris. The pattern of the stroma of the iris could be faintly seen through the hyaline membrane and appeared in places (especially the lower nasal side) to be irregular and fluffy, the normal radial appearance being lost. In some places, chiefly immediately below, the peripheral parts of the superficial radial vessels of the iris came forward and adhered to the deep surface of the hyaline membrane.

The superficial layer of the stroma of the iris was composed of abnormally thick, coarse and sparse golden brown strands, which represented a much thickened peripheral part of the pupillary membrane. They extended to the margin of the pupil and would have overlapped it if the pupil had been dilated. Through the gaps between these strands the deep layer of the stroma could be seen. This was paler and grayish, and rather thinner than normal in that the sphincter could be easily seen through it.

The uveal border at the margin of the pupil was abnormally thick and much puckered. From its upper portion a curious, small, fluffy, whitish mass with a few grains of pigment on its surface hung free by a narrow pedicle and just overlapped the edge of the pupil. It resembled a little mass of organized exudate, but since no other inflammatory signs were present and the mass had no adhesion to the capsule of the lens, it also was probably of congenital origin and represented remains of connective tissue. It could not be true pupillary membrane since it was not continuous with the lesser circle, although, since this lay abnormally near the margin of the pupil, it is possible that it represented a displaced portion.

The second case was that of a girl, aged 8 years. The refraction of each eye was compound myopic astigmatism. Vision equalled 6/36 in each eye. The findings were similar to those in the first case.

In Ballantyne's case, which is also described, there were congenital anomalies of the lids and iris with conjunctival dermoids and subconjunctival lipoma.

Two doubtful cases are added—one reported by Stephenson and one by Coats.

The condition is congenital, and it is in all probability due to an abnormality of the postendothelial tissue occurring at and after the 12 mm. stage. The initial cause of the aberration and also the reason for its assumption of the peculiar appearance described must remain obscure, although the possibility of fetal inflammation acting as the initial cause must be admitted. The article is illustrated.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

UNILATERAL NODULAR INFLAMMATORY REACTIONS OF THE IRIS OF A TUBERCULOUS TYPE: METHYLIC ANTIGEN; CURE. F. ROUSSEAU and J. SPILLMAN, Ann. d'ocul. **170**:328 (April) 1933.

According to the classic treatises on ophthalmology, tuberculosis as an etiologic factor in disease of the uveal tract is not frequently met with; it is rarely noted in scientific literature because the tuberculous nature of a lesion of the iris or

ciliary body is difficult to establish. Observations are given concerning a child, aged 8 years, who had been seen over a period of two years. The clinical examination, local and general, the course of the disease and the efficacy of the treatment by methylic antigen led to the diagnosis of tuberculosis, which the authors believe to be well founded. The history, treatment and course of the disease in this case are given.

McKee, Montreal, Canada. [Arch. Ophth.]

Acquired Amaurosis in the Child. Nahman Cohn, Clin. Pediat. **15**:441 (June) 1933.

A review of the European literature on the subject of acquired amaurosis in children is given in connection with a report of two cases observed by the author. His cases were in children aged 2½ years and 16 months. In the first patient the condition followed a series of tonic-clonic convulsions lasting about half an hour, which occurred in connection with an apparently mild respiratory infection. On recovering from the convulsions, the patient was found to be totally blind. In the other patient the definite time and mode of onset were not learned because of an unsatisfactory history.

Clinical and physical examinations, as well as laboratory tests, gave negative results, with the exception of a positive Wassermann reaction in the first patient. These facts, together with the progressive (though slow) improvement of the condition, led the author to consider both cases of syphilitic origin, in spite of the negative Wassermann reaction in the one patient. Signorelli, New Orleans.

A Peculiar Malformation of the Papilla and Retina. F. Gabardi, Rassegna ital. d'ottal. **2**:117 (Jan.-Feb.) 1933.

The literature on congenital malformations of the disk is reviewed, and a table is given showing all the previously reported cases resembling that of the author. His case was that of a woman, aged 24, with vision reduced to ability to count fingers or less in each eye. The optic disks formed white masses, with indistinct outlines, from which the vessels emerged. White cords extended from these masses to the surrounding retina, the lower half of which was elevated in a number of folds. Other congenital defects were marked dolichocephalism and facial asymmetry and ectopia of the irides and lenses. Previous inflammatory conditions could apparently be excluded, and the author concludes that the findings are to be explained as a congenital defect due to abnormal proliferation of the mesenchyma owing to failure in closure of the fetal cleft. A bibliography is included.

Gifford, Chicago. [Arch. Ophth.]

The Morphology of Human Microphthalmos with Coloboma: Plate Construction Model After Microscopic Serial Sections. R. H. Merrill, Klin. Monatsbl. f. Augenh. **90**:454 (April) 1933.

Microphthalmos, complicated by coloboma, occurs with or without appended cysts which cannot be detected prior to enucleation. The larger the cysts, the smaller is the globe, which may show all the stages from a minute rudimentary eye to anophthalmos. Ophthalmoscopic inspection is impossible in this complication, while the fundus may be observed in cases without orbital cysts, provided the lens is clear. It was one of Merrill's purposes to demonstrate the mechanism of this difference by exact histologic research and by construction of the plate model after microscopic serial sections of the microphthalmic globe of a child, 3 days old. This eye was reduced in size in every dimension; the horizontal diameter of the cornea measured 6 mm.; the optic nerve was very thin and was inserted at the lower half of the posterior portion of the globe. The fetal fissure was open along its entire extension. Retinal or orbital cysts were absent. A. von Szily found these cysts to be secondarily enlarged and to represent everted bags of the retina within the area of the coloboma. The insertion of the optic nerve can be located on the upper (dor-

sal) portion of the globe in microphthalmos coupled with retinal-orbital cysts, and in the lower (ventral) portion in the absence of the cysts. Merrill's research showed that both types represent the terminal result of the same malformation, notwithstanding the different aspect. The difference is brought on by eversion and secondary ectasia of the duplicature of the retina, leading to the formation of orbital cysts, in the one type, and by the direction of the same process toward the interior of the eye, in the other type. The reasons for this mechanism could not be found. It may be due to primary variations of the anlage, especially the differentiation between the retina and the pigment epithelium, and the rôle that they play in the initial formation of the optic cup. The tissues of the anlage forming the margin of the cup turn inward in the one instance and outward in the other. Therefore, it is justifiable to consider the two forms of microphthalmos as one genetic entity with the morphologic distinction between microphthalmos with external, or orbital, cysts and microphthalmos with intra-ocular cysts.

HEIDELMANN, Cincinnati. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

FOREIGN BODY IN THE AIR PASSAGES OF A CHILD AGED 22 MONTHS. JULIAN L. ROGATZ, Arch. Pediat. **50**:589 (Aug.) 1933.

"The case of a male child, 22 months old, is described, in whom the diagnosis of foreign body in the bronchus was made on the physical signs presented. Removal of a piece of nut-meat from the left main bronchus was followed by a short period of fluctuating temperature and a slowly resolving pneumonia, which had entirely cleared one month after bronchoscopy."

WADDELL JR., University, Va.

NASAL NERVE SYNDROME. A. DENTI, Rassegna ital. d'ottal. **2**:32 (Jan.-Feb.) 1933.

The distribution of the nasal nerve, which supplies sensory branches to the globe through the ciliary ganglion and long ciliary nerves and to the sphenoid, ethmoid and nasal mucosa, is described. Attacks of pain with superficial keratitis, cyclitis and iritis, associated with swelling and congestion of the nasal mucosa and relieved by cocainization of the anterior nasal mucosa, have been described by Charlin and others as the nasal nerve syndrome.

The author reports two cases which he considers belong in this group. In one case, a youth of 17 years was subjected to attacks of pain and lacrimation of the left eye associated with rhinorrhea on the left side for a year preceding examination. He was seen by the author during an acute attack of cyclitis in the left eye with left-sided rhinorrhea. Vision was reduced to 1/2. The sinuses were normal. After two applications of cocaine and epinephrine to the anterior nasal mucosa, the attack subsided promptly. Vision one week later was 10/10, and there were no further attacks for three months. In the second case, a woman, aged 20, had attacks of left-sided pain and swelling of the lids for from three to four days before menstruation. During such an attack the cornea and media were unaffected, the pain and a marked edema of the conjunctiva and lids being the only ocular findings. The nasal findings resembled those in the previous case. Three nasal applications of cocaine and epinephrine relieved the symptoms, which did not recur during the following three months.

GIFFORD, Chicago. [ARCH. OPHTH.]

DEVELOPMENT, STRUCTURE AND CHANGES IN THE FORM OF THE HUMAN NASAL SEPTUM IN THE FETAL PERIOD. K. HILLENBRAND, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:1 (May 17) 1933.

Hillenbrand investigated the normal development, anatomy and changes in form of the nasal septum in ninety-three fetuses and newly born infants with the aid of serial sections and reconstruction models. The cartilaginous nasal septum,

the vomer and a part of the intermaxillary bone develop from the median frontal process. They are present in the fetus between 2 and 3 months of age. The fetal cartilaginous septum in its lower portion is held in a groove between the lateral lamellae of the vomer. Anteriorly it lies immediately on the intramaxillary bone. The ossification of the septum commences in the eighth fetal month; it proceeds from the sphenoid sinus. The vomer does not receive its base until later in fetal life. In all specimens a bilateral, physiologic accessory ridge of the cartilaginous septum was noted, which is described in detail. Of the ninety-three noses examined, fifty-seven (61.3 per cent) had an asymmetrical septum; in twenty-four cases the asymmetry resulted predominantly from changes of the vomer, and in the other thirty-three from changes of the cartilaginous septum. The author discusses the pathogenesis of asymmetry of the vomer, deviations of the cartilage and the crest and ridge formation. He discusses the rôle of the physiologic accessory ridges in the development of clinical ridge formation and compares the existing theories for the development of deformities of the nasal septum. From the results of Schwartz' investigation on twins and his own studies the author assumes that most deformities of the septum are determined by the genes.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TEMPERATURE CURVE IN ACUTE OTITIS MEDIA IN A CHILD. LISELOTTE MEYER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:77 (May 17) 1933.

Meyer reports the results of a study of the temperature curves in 200 cases of acute otitis media in children under 14 years of age, and compares them with those obtained by Schiessl in a similar study of 250 adults at the same clinic. Afebrile cases of acute otitis media occur less frequently in children than in adults; subfebrile cases are more frequent, but the majority of the cases are febrile. Pure cases of otitis are in the minority; usually there are primary or concurrent diseases. In nurslings the aural symptoms may be obscured by severe general symptoms. Bilateral otitis is not always accompanied by a higher average temperature, as it is in adults; it may evolve with an insignificant rise in temperature. The general course of the fever in infantile otitis is distinguished by absolute irregularity; light cases may show a high fever and severe cases, slight fever. Frequently deflections in the fever curve have no apparent cause (the individual power of reaction of the organism seems to be the determining factor). An initial high temperature (39 C. [102.2 F.]) in favorable cases shows a lytic drop in a few days; it is usually of a remittent type. A high (from 40 to 41 C. [104 to 105.8 F.]) continuous fever or a fever of long duration points to another disease or a complication; likewise, a too rapidly lowered or a subnormal temperature is an unfavorable sign. Too large or too small daily variations indicate that the disease process is not terminated. Paracentesis in older children usually causes a drop in temperature; in children aged from 1 to 2 years it scarcely affects the temperature. Antrotomy is necessary in children, especially in nurslings, more frequently than in adults. There is usually a lytic drop in temperature after the operation. Complications (sinus thrombosis and meningitis) occur more frequently in children than in adults. In infantile otitis (and sinus thrombosis) there is more frequently an undulating temperature curve without a demonstrable cause. In view of the wide variation in the temperature curve in acute otitis media in children, fever has less value for interpretation of the clinical picture and as an indication for surgical intervention than in adults and may be evaluated only in conjunction with the general and local symptoms.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ROENTGENOLOGY IN GRADENIGO'S SYNDROME: REPORT OF A CASE. H. EPSTEIN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:351 (July 22) 1933.

Epstein examined a child seven weeks after the onset of acute otitis media which was complicated in the third week by the appearance of violent headaches in the frontotemporal region, radiating to the eye, and occasional vomiting. At

the time of examination no clinical manifestation resembling Gradenigo's syndrome remained, but roentgenographically the apex of the petrous bone was lacking and a large defect was visible in its place. These observations, together with the anamnesis, indicated that the otitis had been complicated by Gradenigo's syndrome. The otitis healed after a normal evolution and without surgical intervention. In a roentgenogram taken one year later, the normal configuration of the apex of the petrosa was again visible. A small zone of lesser density appeared over the porus acusticus internus. The author thinks that the defect in the apex of the petrosa may be regarded as a decalcification which probably resulted from the inflammatory hyperemia in the spaces of the middle ear or started from the roentgenologically demonstrated zone of lesser density in the porus acusticus internus. He stresses the discrepancy between the roentgenologic symptoms and the absence of subjective symptoms at the time of examination. He recommends taking roentgenograms of the temporal bone in every case of acute otitis media lasting more than three weeks. Three exposures should be made on the diseased side—one according to Schüller, one according to Mayer and one according to Stenvers (especially suitable for the apex of the petrous bone)—and one control exposure should be made on the healthy side.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

TONSILLECTOMY OR ELECTROCOAGULATION OF THE TONSILS (?). HALLE, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **135**:364 (July 22) 1933.

Halle thinks that electrocoagulation of the tonsils, with its unavoidable discomfort for the patient and its injury to adjacent tissue, should be substituted for tonsillectomy only in cases of hemophilia in which the utmost precautions against dangerous hemorrhages are imperative. In all other cases he thinks that electrocoagulation is contraindicated, especially in view of the fact that the dangers of hemorrhage can be almost eliminated by correct surgical procedure. He has designed two forceps which permit a firm grasp of the tonsil even if it is small and embedded. With these the tonsil may be pulled forward so that not much of the glossopalatine arch need be sacrificed in the excision of the tonsil. The technic is briefly described. If one strictly avoids using the instruments intended for holding the tonsil for handling other tissues or vessels, infection need not be feared, especially if an antiseptic powder is sprayed in the tonsillar fossa after operation.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

PATHOGENESIS AND THERAPY OF ALLERGIC INFLAMMATION OF THE ACCESSORY NASAL SINUSES. A. GLASSCHEIB, Monatschr. f. Ohrenh. **67**:565 (May) 1933.

Glasscheib says that the allergic catarrhal inflammation of the nose, which is characterized roentgenologically by edematous swelling of the mucosa of the maxillary sinus to the point of polypus formation, has its origin in a purulent inflammation of the maxillary sinus. Some of the pus secreted by the mucosa is resorbed, especially when there is stasis, and with it the toxins and products of protein decomposition from the disintegrated bacteria. These constitute antibodies; the union of antigen and antibody leads to the development of allergy within about eight days. The reaction of the secretion is alkaline instead of acid as in most allergic secretions, but the eosinophilic reaction of the tissue of the mucosa and the polypi, as well as that of the blood, is a certain sign of allergy. This theory of pathogenesis has a therapeutic interest. In the treatment of acute suppuration of the maxillary sinus, resorption of the pus should be prevented by aspiration or irrigation. If an allergic inflammation develops, desensitization with albumin should be instituted. The administration of acid may also be tried. If the polypi do not regress with this therapy, curettage may be tried, followed by desensitization. The inflammation usually extends to the ethmoid, frontal and sphenoid sinuses, but is most easily recognized in the maxillary sinuses. The disease passes imperceptibly from the acute to the chronic stage, and its early recognition is therefore all the more important.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

CONGENITAL ATRESIA OF THE LARYNX. E. FRITZ, Virchows Arch. f. path. Anat. **289**:264, 1933.

The anomaly described occurred in a new-born male infant 43 cm. in length. Heart tones were heard for from twelve to fifteen minutes after birth; the application of cold water led to a single spasmodic attempt at respiration. The larynx appeared normal externally, and the epiglottis was normal. The superior opening of the larynx was normal, but at a distance of 0.5 cm. below the opening the larynx was closed. The trachea was absent for a distance of 3 cm. below the larynx. The bronchi and a portion of the trachea 1.5 cm. long superior to the bifurcation were normally formed. A narrow fistula connected the esophagus with the lower portion of the trachea. The generalized edema and hypertrophy of the lungs that previous observers have noted in atresia of the larynx were apparently not present in this instance. SCHULTZ, Evanston, Ill. [ARCH. PATH.]

SURGICAL TREATMENT OF CONGENITAL LARYNGEAL DIAPHRAGM. G. KRIEGSMANN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **33**:218 (June 8) 1933.

In a woman, aged 25, who had always had a hoarse voice and who complained of dyspnea, Kriegsmann found a membrane extending from the front of the glottis and obstructing almost two thirds of it. The grayish-white, somewhat translucent membrane did not affect the motility of the vocal cords. Following excision of the membrane by cutting along the free edges of the vocal cord an improvement in breathing was observed, but the voice was completely aphonic, and a fibrinous exudate containing some cellular elements appeared in the glottis, which had to be removed by curettage. The exudate continued to reappear despite all efforts to prevent it, and a membrane of almost the same size as the first one developed within twenty-three days. An incision of the new membrane between the vocal cords and coagulation of the surfaces of the wound by surgical diathermy cleared the glottis and relieved the dyspnea, but five weeks later a new membrane, slightly less extensive than the original one, had formed. The voice was still aphonic, and the dyspnea had returned. After a twice repeated sharp incision of the membrane in the median line, the tendency to adhesion and reconstitution of a membrane was somewhat restrained, and the patient was dismissed with fair results. Epithelization of wound surfaces in places not previously covered with epithelium is hard to obtain. Surgical therapy for a congenital laryngeal diaphragm is recommended only if urgent indications exist. If the membrane is thin toward the back, as in this case, a median incision of the thin portion is advised. If the membrane is thick, the larynx should be opened to permit postoperative treatment after division of the membrane and until the final result can be seen.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ROENTGENOLOGIC DIAGNOSIS AND THERAPY OF CONGENITAL OSSEOUS ATRESIA OF THE EXTERNAL AUDITORY MEATUS. R. MITTERMAIER, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **24**:213 (July) 1933.

Mittermaier successfully constructed an artificial auditory canal in the left mastoid antrum of a girl, aged 20, with bilateral congenital imperforation of the auditory meatus. The left side was chosen for operation because the head of the malleus was visible on the roentgenogram of this side whereas it was missing on the right side. The degree of malformation, according to statistics, is usually less in cases in which the malleus and incus are present. In most cases in which operation has been successful, ossicles were present; improvement was slight or lacking when they were absent. The patient's hearing on the side operated on was greatly improved for vowels of the lower register (*C* to *C* 2), and she was able to understand conversation at a distance of 5 meters, as contrasted to from 1 to 2 meters prior to operation. Operation is indicated only if two conditions are fulfilled. In the first place, the baryecoia must be primarily a defect of con-

ductivity. This can be determined by functional tests, especially the audiometer curve and the test for vowel hearing. If there is a pronounced labyrinthine baryecoia, the creation of an air passage is ineffective. In the second place, the presence not only of an antrum but of the tympanic cavity with its organs must be considered, and the ossicles, at least the head of the malleus, should be roentgenographically demonstrable. The author recommends the axial exposure of the temporal bone for this purpose.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

QUESTION OF TONSILLOTOMY IN CHILDREN. K. GERLOFF, Ztschr. f. Laryng., Rhin., Otol. (Teil 1: Folia oto-laryng.) **24**:255 (July) 1933.

On the basis of examinations made several years after tonsillotomy in 110 children, Gerloff concludes that the uniform substitution of tonsillectomy for tonsillotomy is not justifiable. Since 76 of the patients became free from symptoms after tonsillotomy, this operation must still be considered preferable to tonsillectomy, which is a much more extensive intervention and one which deprives the child of a valuable organ. Tonsillotomy is the method of choice in cases involving pure hyperplasia of the tonsils. The anamnesis is of great value in determining whether pure hyperplasia or one of inflammatory origin exists. In the former case tonsillotomy is almost always entirely successful; in the latter case, the result is frequently unsatisfactory. Tonsillotomy should be avoided when the anamnesis and symptoms leave no doubt as to the inflammatory origin of the tonsillar hyperplasia, as examinations have shown that chronic tonsillitis in early childhood is sometimes unfavorably influenced by tonsillotomy. In such cases climatic or medicinal therapy should be tried, in an attempt to preserve the tonsils, which are necessary for the general immunity of the youthful organism; but in the presence of severe symptoms or at the first appearance of manifestations of central decompensation, tonsillectomy must be employed.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Surgery and Orthopedics

APPENDICITIS IN CHILDREN. CONRAD J. BAUMGARTNER, Arch. Pediat. **50**:571 (Aug.) 1933.

One hundred consecutive cases of appendicitis in children are reviewed with the view of determining some of the outstanding features of the history, physical examination and laboratory findings. Of 100 cases in which there was surgical intervention, the diagnoses were: chronic appendicitis, 8; subacute appendicitis, 2; acute appendicitis (not ruptured), 35; acute appendicitis (ruptured), 55. It appears that chronic appendicitis is rare in children as compared to adults. In the cases of chronic appendicitis occurring in this series, about one third gave a history of recurrent attacks. The high incidence of perforated appendix in young children appeared to be due primarily to delay.

Attention is called to the fairly frequent association of sore throat, of infection of the middle ear and of colds with appendicitis, often leading to a mistaken diagnosis. Tenderness in the right lower quadrant was the most constant physical finding, being present in 94 per cent of acute and 80 per cent of chronic cases. Rigidity of the rectus muscle occurred in about the same proportion in cases in which perforation occurred, but less frequently in the simple acute cases. The temperature as a rule was not high, averaging 101.2 F. rectally. The average white cell count in cases of acute appendicitis without perforation was 16,696, as compared with 20,432 in the cases with perforation. It would seem that a white cell count above 20,000 in a suspected case of appendicitis pointed to a ruptured appendix. Attention is called to the fact that a young child is not able to recognize pain accurately, usually simply complaining of abdominal pain. Baumgartner believes that this fact contributed to the delay in operation in many cases. Almost one half of the cases of appendicitis with rupture were seen in children under 5 years of age, and of these only 10 per cent were seen within the first twenty-four hours.

WADDELL JR., University, Va.

CONGENITAL HERNIA OF THE OVARY AND TUBE INTO THE CANAL OF NUCK WITH REPORT OF A CASE. A. E. HARBESON, Canad. M. A. J. **29**:295 (Sept.) 1933.

The author reports a case of hernia in the canal of Nuck in a baby 2 months of age. An operation was performed when the baby was 11 weeks old. The ovary, fallopian tube, and infundibulopelvic ligament and a short loop of the sigmoid colon were found in the sac. The recovery was uneventful. MOORE, Omaha.

NON-OPERATIVE VERSUS OPERATIVE TREATMENT OF TUBERCULOSIS OF THE SPINE IN CHILDREN. J. H. KITE, South. M. J. **26**:918 (Nov.) 1933.

Kite reports that spontaneous fusion of the diseased vertebral bodies, which is nature's method of curing tuberculosis, occurred in only 2 per cent of his cases. The deformity should be corrected as much as possible before operation. Absolute immobilization is the most important prerequisite in the treatment of any tuberculous lesion. No type of mechanical support will give absolute immobilization. This can be obtained for the diseased bodies of the vertebrae only after the posterior portions of the vertebrae have been firmly ankylosed by bony fusion. In evaluating the results, one must distinguish between adequate and inadequate operations. All cases having an adequate operative fusion showed a solid bony ankylosis of the diseased bodies about three years after operation.

Great care should be exercised to prevent operative shock, as patients with tuberculosis do not undergo operation as well as healthy patients. Besides the immediate risk, there is the additional hazard of lowering the patient's resistance and thus disposing him to a later flare-up of tuberculosis elsewhere in the body. For this reason it is recommended that if more than two vertebrae are diseased, the operation be done in two stages. For the same reason it is further recommended that the operation be done under local anesthesia.

Bony fusion in the operative area and bony ankylosis of the diseased bodies occur as rapidly in children as they do in adults. Mechanical support should be continued until the diseased bodies show solid fusion.

Of forty patients treated by the nonoperative method, one showed an excellent result, and seven, satisfactory results; fourteen were somewhat improved; eleven were unimproved, and seven died. In fifty patients treated by the same method plus operation, the results were as follows: Of thirty-four who had adequate operations, all showed excellent results; of fifteen who had inadequate operations, one showed an excellent result, six, satisfactory results, and six, poor results, and two died; one patient died during the operation. While surgical intervention does shorten treatment, it affords no excuse for neglecting to use everything of value in the conservative treatment, both before and after the operation.

Operative fusion is done only to cure tuberculosis, and this it will do in most cases, if an adequate procedure is followed and if adequate postoperative treatment is given. SCHLUTZ, Chicago.

INTESTINAL INVAGINATION IN INFANCY. HUGO FORTES, Arch. de pediat., Rio de Janeiro **5**:327 (July) 1933.

The author reports 2 cases of intussusception in infants 18 months and 7 months of age, respectively. He quotes the statistics of Moynihan in which in 114 cases the mortality, when resection was not necessary, was 23.7 per cent, whereas in 29 cases that had existed long enough to make resection necessary the mortality was 89.6 per cent. SANFORD, Chicago.

THE TIME OF SURGICAL INTERVENTION IN CONDITIONS CALLING FOR OPERATION IN CHILDHOOD. J. TRENCHS CODONES, Paidoterapia **12**:311 (Aug.) 1933.

The exact time to operate in conditions in which operation is advisable in children is a question of great importance because on it often depends the life

of the child as well as the success of the operation. The time varies in each case, being dependent on the symptoms and on the age of the patient.

According to Codones, chloroform is still the anesthetic of choice in about half the cases reported. He suggests the following ages for the different operations: harelip, the first few days of life; cleft palate, between the first and the second year of life, because phonation will be more perfect; congenital dislocation of the hip, if unilateral, before the age of 2 years, and if bilateral, before the age of 5 years; syndactylism, the first few years of life; appendicitis and empyema, as soon as the diagnosis is made. Spina bifida should not be operated on if the herniation includes the cord, but if it is of moderate size or is only a small tumor without symptoms operation may be done up to 2 years of age; hydrocele is operated on before the age of 2 years; phimosis, rather late, about the age of 6 months; hypospadias and epispadias and extrophy of the bladder are not operated on until about the eighth year of age; undescended testicle is operated on before the age of 6 years. Acute osteomyelitis requires early surgical intervention.

HERRON, Spokane, Wash.

ORTHOPEDICS OF BATH TREATMENT OF THE HEINE-MEDIN DISEASE IN THE REPARATION STAGE. FRANK KORNMANN, Schweiz. med. Wchnschr. **63**:373 (April 22) 1933.

The degree of postparalytic crippling depends on contracture much more than on the paralysis. Contractures are avoidable. Certain signs precede the appearance of paralysis: pain in the psoas muscles on bending the lumbar vertebrae, the Kernig sign, premonitory muscular weakness, diminished respiratory activity of the ribs and hypotonia. Hydrotherapeutic treatment should be instituted when the reparative stage is reached, usually months, only exceptionally in one month, after the paralysis becomes fixed. Complete rest and stretching must be adjusted properly. The earliest contractions in paretic muscle groups should take place voluntarily during the bath and should not be forced artificially by walking. Balneotherapy may be accorded a more active place in the second period of repair if the paralysis steadily improves and danger of involving allied muscle groups diminishes. The author particularly advises swimming in warm water, for then the overbalancing of antagonists is restrained by swimming belts and air cushions. Electric baths and prolonged warm baths are of service. Overworked paralyzed muscles never regenerate, but paralyzed muscles which are stretched may improve after the lapse of years in spite of severe initial paralysis.

VINTON, Brooklyn.

Miscellaneous

DENVER'S INFANT MORTALITY. F. P. GENGENBACH, J. Pediat. **3**:718 (Nov.) 1933.

The high mortality of infants in Denver was studied for one year. The highest mortality was found in those parts of the city in which conditions of housing and sanitation were the poorest. The families with the lowest incomes also showed the greatest infant mortality. The rate was definitely much lower when the mothers had received adequate prenatal medical care. The rate was highest in children whose mothers were under 20 years of age. The causes were in order of frequency as follows: prematurity, pneumonia, diarrhea, congenital malformations and injuries received at birth.

LEMASTER, Evanston, Ill.

JACOB HEINE AND HIS CONTRIBUTION TO POLIOMYELITIS. JOHN RUHRÄH, J. Pediat. **3**:765 (Nov.) 1933.

Jacob Heine's pioneer studies on the treatment of poliomyelitic paralyses are discussed. A clinical description of the disease is quoted from Heine's monograph published in 1840. In the treatment he made a great step forward in recommending not only the treatment of the deformities but also their prevention by the use of rubber bandages or wire and leather apparatus.

LEMASTER, Evanston, Ill.

WHAT THE PEDIATRICIAN CAN DO FOR DENTAL CRIPPLES. CLEOPHAS P. BONIN, New England J. Med. **209**:875 (Nov. 2) 1933.

An interesting and well illustrated presentation of the subject is given. Bonin does not believe that early orthodontic treatment will cause a child's nervous system to become upset. One case is reported in which treatment was started between the ages of 3 and 4 years with excellent results. The continued open mouth and sagging lower jaw, usually caused by enlarged adenoids and tonsils, upset the equilibrium of the forces of the facial muscles, with later faulty development of the bones of the face. A similar result has been proved experimentally on a dog by early occlusion of one side of the nose. One case illustrates the possibility of increasing the size of the posterior nares by appropriate treatment. A timely plea is made for the early cooperation of the pediatrician, rhinologist and orthodontist.

GENGENBACH, Denver. Colo.

ABSORPTION OF INFRA-RED RADIATION BY THE HUMAN BODY. B. D. H. WATTERS, Brit. J. Phys. Med. **8**:74 (Sept.) 1933.

Watters reviews work done by several investigators on the transmission and absorption of infra-red radiation.

HARTMAN, Cleveland

THE FIELD OF THE LIGHT DEPARTMENT IN A GENERAL HOSPITAL. A. E. RAYNER, Brit. J. Phys. Med. **8**:76 (Sept.) 1933.

Rayner shows several "before and after" photographs of conditions that are, perhaps, not generally recognized as being especially amenable to light treatment, such as extensive burns, indolent and suppurating ulcers and certain common diseases of the skin. He outlines his technic of treatment and remarks that the most constant feature is the rapid relief of pain.

HARTMAN, Cleveland.

CONDITION OF THE GUMS DURING THE FIRST DENTITION. A. G. ALARCON, Nourrisson **21**:232 (July) 1933.

Preceding the eruption of the first teeth, babies commonly bite on any objects that come into their hands. Alarcon believes that this is done, not on account of pain or discomfort in the gums, but simply as a manifestation of the early development of the muscles of mastication aggravated by the generalized muscular hypertonicity characteristic of young babies.

MCCLELLAND, Cleveland.

REVIEW OF INFANTS' DISEASES FOR 1933. P. LEREBOULLET and F. SAINT GIRONS, Paris méd. **2**:341 (Nov. 4) 1933.

This article is the annual review of the French literature on infants' diseases. Subjects reviewed are infant welfare, nutrition and infant feeding. An interesting item under the head of feeding is an authentic case of anaphylaxis of an infant to its mother's milk, reported by Leveuf and Vignes before the Paris pediatric society. Much space is given to the efficiency of vitamin A as an anti-infective agent. Busson believes that this has been greatly overrated. There is considerable discussion of the anemias of infancy, Schüller-Christian's disease and infantile diabetes. In this connection, Lereboullet published a recent article in *Progrès médicale*. This is an excellent résumé of the French literature on infancy for the past year.

SANFORD, Chicago.

PROTECTION OF INFANCY IN A SUBURBAN COMMUNITY. G. ICHOK, Rev. franç. de puéricult. **1**:106 (May) 1933.

In the city of Clichy, taken as an example of a small city in which rapid growth and industrial development have caused overcrowding and a smoke laden atmosphere and in which many of the mothers are employed, the problem of

child health is a serious one. Such organizations as the crèche and the maternal school, school lunchrooms, vacation homes, playgrounds, municipal dispensaries for medical care and programs of public education cooperate to protect the children, as far as is possible under present economic conditions, from the bad effects of poor home surroundings and ignorant care.

CRANE, Chicago.

LIFE IN THE OPEN AND SEA BATHING FOR CHILDREN OF THE CITIES DURING THE SUMMER MONTHS. ARVID WALLGREN, Rev. franç. de puéricult. **1**:149 (June) 1933.

In Gothembourg, Sweden, an opportunity for a summer vacation is provided for the children who would otherwise spend their summer in the hot city. Each day a train load of children of all ages is taken a short distance from the city to a protected spot on the shores of a shallow bay. Here the children play all day with a minimum of supervision. Instructors in gymnastics and swimming are present to teach those who want to learn. The municipality provides railroad transportation and milk for each child and pays the supervisors, while the children bring their own lunches. From three to five thousand children make this excursion daily.

CRANE, Chicago.

REMARKS ON THE DEMOGRAPHIC METHOD APPLIED TO INFANCY AND ON STATISTICAL TECHNIC. R. H. HAZEMANN, Rev. franç. de puéricult. **1**:154 (June) 1933.

Methods of applying correct technic in deriving statistics dealing with infancy are described and illustrated.

CRANE, Chicago.

THE CHILD WELFARE MOVEMENT IN BELGIUM. C. COHEN, Rev. franç. de puéricult. **1**:174 (June) 1933.

L'Œuvre Nationale de l'Enfance was created in Belgium in 1919. It provides prenatal clinics, maternity homes, visiting nurses, child placement bureaus, crèches, and cantines, but the chief branch of its activity is the maintenance of clinics for infant feeding.

CRANE, Chicago.

CLIMATOTHERAPY IN CHILDHOOD. R. DEBRE and E. CHABROL, Rev. méd.-sociale de l'enf. **1**:92 (April) 1933.

The relative advantages of seaside and mountain are discussed in relation to different constitutional make-ups and to different disease conditions. Debre and Chabrol do not agree completely with the old conception that the high-strung child with a relatively unstable nervous system is better off in the mountains, while the phlegmatic child needs the stimulating effect of the sea. Individual reactions and the type of life adopted must also be considered. Tuberculosis of the skin and bone is overcome best on the seashore, while that of the lungs and pleura is better treated in the high altitudes of the mountains. For rickets, the evidence is in favor of the seashore, where, in addition to the sunlight, the child may have the benefit of warm salt baths. For convalescent children and for those with anemia, contagion must be avoided; either the low plateaus of the Alps or a protected sea-coast is suggested.

LESLIE, Chicago.

INFLUENCE OF THE p_H ON THE TOXICITY OF SODIUM TAUROCHOLATE. P. SCHIAPARELLI, Riv. di clin. pediat. **31**:461 (April) 1933.

Schiaparelli, in a previous article, showed that the minimum lethal dose of sodium taurocholate for rabbits was 0.5 Gm. per kilogram of body weight, when administered intravenously, and 0.12 Gm. when given intrapleurally. Changing the p_H of the sodium taurocholate from its usual figure of 5.8 to 7.4 did not affect

the minimum intravenous lethal dose but somewhat increased the intrapleural dose. The author has not determined whether the power of the drug to dissolve bacteria or a purulent exudate is affected by the changing of the p_H.

HIGGINS, Boston.

CONTAMINATION OF THE WATER OF SWIMMING POOLS BY URINE. A. MAHLA, Arch. f. Hyg. **110**:231 (July) 1933.

The best method of determining the quantitative contamination of the water of swimming pools by urine was found to be by estimation of the increase of nitrates in the water. Specific urinary substances, such as uric acid and creatinine, could not be demonstrated. Errors due to cutaneous secretions, desquamated epithelium and foreign matter are negligible if the bathers are required to take a shower before entering the pool. The average amount of urinary contamination was found to be about 60 cc. per bather. As the average quantity of urine passed by one person is about 300 cc., it is estimated that one bather out of every five empties his bladder into the swimming pool. The colorimetric reaction of van Griess, the details of which are given, is suggested as a practical means of checking the dilution of the water of the swimming pool by urine.

The abstractor wonders whether similar studies have been made in this country. An increase of urine in American swimming pools since the return of beer and other alcoholic beverages might add one more argument to the long list in favor of prohibition.

GLASER, Rochester, N. Y.

CORRELATION OF THE CLINICAL PICTURE OF LEAD POISONING WITH THE LEAD CONTENT OF BLOOD IN URINE. E. BASS, Deutsche med. Wchnschr. **59**:1665 (Nov. 3) 1933.

Boss stresses the significance of quantitative determinations of lead in the blood and urine of patients who show clinical signs of lead poisoning or who are suspected of having lead poisoning. He advises the electrocolorimetric method of Schmidt and Weyrauch for quantitative analysis. However, 100 cc. of blood and 1,000 cc. of urine are necessary for this test.

Boss thinks that if the lead content of 100 cc. of blood is more than 0.06 mg. or if the lead content of 1,000 cc. of urine is more than 0.1 mg., one usually is able to find clinical signs of lead poisoning. He describes forty cases of adults on whom the method of Schmidt was used. Twenty-four were suspected of having lead poisoning. Thirteen had clinical signs of the disease, and three had had a previous diagnosis of lead poisoning. Those suspected showed normal values for lead. The three patients who had had lead poisoning showed a slight elevation of the lead content of the blood and urine. However, the thirteen patients who had clinical symptoms showed high values. The clinical signs among the thirteen cases in which the condition had been definitely diagnosed and in which there was a high lead content in the blood and urine were as follows: colic in ten, anemia in seven, stippling in five, porphyrinuria in five and neurologic signs in four. Boss stresses the significance of taking into consideration both the clinical and the laboratory findings.

KERESZTURI, New York.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Scientific Sessions, Asheville, N. C., May 3-5, 1934

CHARLES A. FIFE, M.D., *President, in the Chair*

First Session

Thursday Afternoon, May 3

PRESIDENTIAL ADDRESS: THE CHILD'S FAMILY ADVISER. DR. CHARLES A. FIFE, Philadelphia.

This article was published in full in the July 1934 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, p. 1.

THE PITUITARY SEX HORMONES. DR. PHILIP E. SMITH (by invitation), New York.

The problem of pituitary physiology has become much more complex than could be anticipated at the beginning of the period of active work in this field some ten years ago. Work with anterior pituitary extracts has revealed the presence of a number of hormones in this gland. In addition to the male and female sex hormones, there are at least two gonad-stimulating hormones found in the urine, the site of formation of which has not been definitely established. These urinary gonadotropic substances still further complicate the problem.

The action of gonad-stimulating extracts from the anterior lobe of the pituitary gland, and from the urine of pregnant women, of women who have been castrated and of those past the menopause is discussed, with special emphasis on the urinary principles. Evidence shows that the extracts from the urine of pregnant women act predominantly on the connective tissue constituents of the gonads, whereas those from the urine of castrated women or of women past the menopause affect the germ cells predominantly. The action of these two urinary extracts is discussed primarily from the experimental point of view, though deductions of possible clinical value are mentioned.

The opposite phase of the subject—the capacity of tissues or organs to respond to hormonal therapy—is also discussed. Evidence on this question is still scanty, and this phase has not received the consideration which it merits. Aging of the reproductive organs modifies their response. This aging varies not only in different persons but probably also in different organs of the same person. A knowledge of the variability in development is of importance in judging the need and effectiveness of treatment.

ATROPINE. DR. J. D. PILCHER, Cleveland.

The cause for the occasional tolerance of atropine by infants and young children has not been determined. The blood serums of rabbits tolerant to atropine inactivate this drug. In this work serums of rabbits inactivated from 1 to 20 mg. of atropine per cubic centimeter—that is, up to 2 per cent of atropine.

The serums of some 70 nontolerant infants and of a few tolerant infants were thus examined. The simplest method was found to be that of observing the mydriatic effect of atropine on the cat's pupil and comparing this with the effect of mixtures of serums with atropine of various strengths that had stood several

hours. The most tolerant subject was a 2 year old Negro boy, who received three doses of 5.5 mg. of atropine sulphate by mouth in one day and two doses of 5 mg. subcutaneously at intervals of four hours. Deep sleep and a somewhat increased heart rate were the only signs of the action of atropine.

None of the serums of these tolerant subjects showed any inactivating action on atropine; in fact, when the serums of some of these infants, as of some of the controls, were mixed with the atropine the latter had a somewhat greater mydriatic effect, a result which has been reported by another observer.

There is a little evidence that atropine is destroyed in the body, as the urine of the boy just mentioned yielded far less atropine after large subcutaneous doses than did a similar quantity of urine to which a similar quantity of atropine had been added.

Dilutions of atropine commonly used in practice—a 1 : 1,000 solution—are said to deteriorate rather rapidly, yet several such samples lost little of their potency when kept for two years at room temperature. This result was determined by the action on the cat's pupil, on infants and on the cardiac endings of the vagus nerve in the rabbit.

DISCUSSION

DR. D. MURRAY COWIE, Ann Arbor, Mich.: I have been particularly interested in the effect of atropine on the gastro-intestinal gradient. In the normal rabbit the rate of the excised intestinal segments contracting in oxygenated Locke's solution is never increased by the addition of atropine to the bath. The tone and the amplitude of contraction are decreased in all the segments. When one adds pilocarpine to the bath in small, gradually increasing amounts, there is a slight rise in the tone of all the segments, reaching a maximum above which the further addition of pilocarpine produces no change. If small amounts of atropine are added to the bath all at one time, there is a marked rise in the tone of all the segments, which is sustained for from thirty to forty minutes. The tone is increased first in the duodenum, then in the upper part of the ileum and last in the lower part of the ileum. If large amounts of pilocarpine are added to the bath all at one time, there is a more marked rise in tonus, causing a decrease in amplitude and a cessation of contraction. After a certain number of minutes there is gradual recovery. The circular muscular contractions are influenced early by pilocarpine. Both the segmenting and the traveling varieties of contraction are markedly affected.

When atropine is added to the bath in which fresh intestinal segments are contracting, as I said before, there is little or no effect. On the other hand, if the atropine is added after pilocarpine has been operating, the function of the segments, both longitudinal and circular, is reduced to normal. This recovery is first noted in the duodenum, then in the upper part of the ileum and last in the lower segments of the ileum.

If the atropine is added to the bath gradually, the return to normal is orderly and gradual. If it is given in large amounts all at one time, the tonus of the segments falls below the normal control tracing; circular contractions cease for a while; then the tonus slowly increases, and the contractions again become normal.

After the intestinal segments have been acted on by these two drugs, even if considerable time is given for them to recover, they seem to be refractory; that is, they remain resistant to these drugs.

The large amount of atropine sulphate that is necessary to overcome enterospasm is surprising. In a young boy [a slide is shown] 0.1 grain (0.06 Gm.) a day over long periods of time was required to stop the painful spasm. So long as large amounts were given, the patient was able to eat normally and made marked gains in weight. Finally atropine was no longer necessary.

I had the opportunity to study a case of enterospasm in a woman [a slide is shown] who required between 0.3 and 0.4 grains (0.02 and 0.025 Gm.) of atropine sulphate a day over long periods of time to control the pain (controlled observation). There was never any manifestation of overdosage. The eyes were kept under the observation of an ophthalmologist. Finally, the greater and lesser splanchnic nerves and the white rami were cut on both sides from the sixth to

the eleventh dorsal segment. It is now several years since the operation and, of course, there has been no return of the symptoms.

After observing the effect of atropine in hypertonic infants and seeing that it relaxed the striated as well as the smooth muscles, I tried its effect on a physician's baby, aged 10 weeks, with marked wryneck, who was brought to the hospital for surgical consideration. This infant had a high tolerance for atropine. On proper dosage the spasm of the sternocleidomastoid relaxed. The atropine was continued for a few months, and, as in the hypertonic infant, was finally found to be unnecessary.

CERTAIN TYPES OF ICTERUS GRAVIS. DR. S. G. ROSS and DR. T. R. WAUGH (by invitation), Montreal, Canada.

The study of a number of new-born infants suffering from severe jaundice led the authors to believe that these cases can be classified into fairly well defined groups. This study does not include the well recognized types due to gross obstruction in the large bile ducts, to sepsis or to congenital syphilis. Apart from these, it seems possible to recognize the following types: (*a*) jaundice which is primarily hemolytic; (*b*) jaundice which is primarily hemolytic, but which has an added obstructive (regurgitation) factor, and (*c*) jaundice which is primarily obstructive and in which the hemolytic factor is either absent or slight.

Icterus gravis resulting from marked hemolysis in the first few days of life (and probably also in intra-uterine life) is the most common type. It is often familial. It results in severe anemia and is characterized by the presence in the circulating blood and in the blood-forming organs of many immature forms of blood cells, both red and white. The authors object to the use of the term "erythroblastosis of the new-born" for this type for the following reasons: (*a*) The presence of immature red cells is a temporary phase. (*b*) This phenomenon seems to be an effort on the part of the hematopoietic system to supply the loss of red blood cells occasioned by the severe hemolysis which has taken place. (*c*) Any severe hemolytic anemia in infancy may result in a temporary outpouring of embryonic blood cells into the circulation.

In most cases of icterus gravis which we have seen the jaundice was the result of hyperbilirubinemia due to hemolysis, plus regurgitation of bile pigment resulting from block of the bile canaliculi with bile pigment. In some cases obstructive jaundice persists after the hemolysis ceases. In others, the obstruction passes off, but the hemolysis persists and causes continuation of the jaundice.

Cases of the third type are less frequent. The jaundice is purely obstructive, and no anemia develops. The patient is less severely ill; the jaundice is usually not so severe, and the prognosis is better.

CURE AND PREVENTION OF RICKETS IN PREMATURE INFANTS WITH TUNGSTEN FILAMENT RADIATION. DR. HENRY J. GERSTENBERGER (by invitation), DR. ARTHUR J. HORESH (by invitation), DR. G. R. RUSSELL (by invitation) and DR. A. L. VAN HORN (by invitation), Cleveland.

As a result of the studies carried out at the Babies and Childrens Hospital of Cleveland during recent years in an attempt to decide whether dual purpose lighting is a feasible method of transmitting an adequate amount of the antirachitic factor to man, we have realized more and more that the required dose of the antirachitic factor administered through the skin of human infants in the form of ultraviolet light from this source is extremely small. On this basis, it was considered probable that it would be possible to use a continuous light bath from tungsten filament lamps of small wattage emitting the specific wavelengths, as a satisfactory source of both heat and antirachitic rays.

The present report includes observations made on 7 premature infants. Three of the infants were rachitic, and in them the curative value of the light was studied. In the remaining 4 infants its preventive efficacy was estimated. Three of these infants were definitely not rachitic. The fourth also was not considered to be

rachitic; however, the rather high phosphatase level in this infant suggests that possibly rickets was developing.

During the period of observation 6 of the 7 infants received the same food, which was a mixture of equal parts of whole and skimmed cow's milk, with lactic acid added in the proportion of 5 cc. to the liter and with carbohydrate in amounts sufficient to meet the caloric requirements of the individual infant. The seventh infant was fed his own mother's milk. Orange juice in sufficient quantities was given to all the patients. Saccharated carbonate also was administered daily, in most cases in a dose of 0.5 Gm. three times per day.

Each infant was put in a bassinet, on the sides of which an ordinary surgical cradle was placed. On the under surface and in the center of this cradle a reflector was fastened, to which was attached a cluster of four 30 watt, CX Mazda bulbs. The lamps were guarded by a wire mesh screen attached to the sides of the reflector. The cradle and the sides of the bassinet were closed in all around by a double layer of bed sheeting for all the surfaces except the front of the cradle, where a curtain of Shaker flannel was used. In the bottom of this curtain was an opening through which the infant's head projected, to prevent its exposure to the lights and to enable the infant to breathe the air of the room or ward. The infants were naked, except for the diaper area, which was covered by the ordinary napkin.

The number of bulbs burning varied according to the temperature requirements of the individual infant. However, one bulb was kept lighted continuously, and only rarely were all four bulbs lighted at the same time. For the greater part of the time, not more than two bulbs burned.

The distance of the bulbs from the mattress level of the bassinet was 35 cm. The reflector used was 34 cm. long, 22 cm. wide and 9 cm. deep. The outer side of the reflector was covered with asbestos and the under side with aluminum paint.

Roentgenograms of the left wrist were taken at weekly intervals, and the calcium, inorganic phosphate and phosphatase levels of the blood serum were determined approximately every four weeks.

Tables show that a continuous light bath produced by 30 watt, CX Mazda bulbs used in the manner outlined is adequate for the prevention and cure of rickets in premature infants who are growing well, provided that at least one of the bulbs is kept burning continuously and that additional bulbs are lighted to meet the temperature requirements of the infant. In this study the average number of bulbs used was approximately two, the emitted light of which, according to measurements and computations made by A. H. Taylor (Lighting Research Laboratory, Nela Park, Cleveland; director, Dr. M. Luckiesh), represents in ultraviolet intensity approximately forty seconds of midsummer noon sunlight daily.

At the same time the light bath, as used in this study, served as an excellent source of heat for these infants, enabling them to maintain a satisfactory body temperature without much difficulty.

DISCUSSION

Dr. Isaac A. Abt, Chicago: Forty or fifty years ago physicians were discussing whether craniotabes was due to syphilis or rickets or to both. Dr. Gerstenberger, an eminent authority on rickets, now informs us that craniotabes may occur without associated rickets. I should like to ask him if this occurs with considerable frequency.

Has Dr. Gerstenberger, in his wide experience, observed that craniotabes improves under the administration of vitamin D factors concomitantly with the general improvement that occurs in other parts of the body in rickets?

Are the lamps which Dr. Gerstenberger has referred to of sufficient strength to irradiate milk, thus increasing the vitamin D factor?

Dr. Julius H. Hess, Chicago: Were the older babies, some of which were as old as 9 months, kept exposed constantly throughout the whole day to get their forty seconds of average sunlight, or were they removed from the crib at night?

DR. HENRY GERSTENBERGER, Cleveland: They were exposed continuously to at least one lamp during the entire period.

I have seen physiologic cranial tabes disappear in an infant who received no antirachitic factor, but simply a dilution of milk, and I have seen cranial tabes develop in human infants who received cod liver oil and in addition were irradiated with light from a potent lamp.

It is believed by some investigators that the children of the so-called intelligentsia are more disposed to physiologic cranial tabes than other types of infants. Whether this is so I do not know. But there is no question in my mind that cranial tabes may develop when there is no rickets.

I am sure that these lamps would not be adequate for the irradiation of milk. Carbon arc lamps are being used for the irradiation of milk at present.

EFFECT OF ACUTE DISEASES ON THE REACTION OF THE SKIN TO TUBERCULIN. DR. A. GRAEME MITCHELL, DR. WALDO E. NELSON (by invitation) and DR. THOMAS J. LEBLANC (by invitation), with the assistance of ESTELLE W. BROWN, B.S. (by invitation), Cincinnati.

Figures obtained from the present study have been combined with those of previous studies already reported by the authors. In all instances the same type and same dosage of tuberculin were employed in the patient before, during and after the acute period of the disease.

*Rates of Reaction to Tuberculin During the Febrile and Convalescent Stages of Acute Diseases**

		Positive Reaction to Tuberculin Test				$\frac{K}{PE_K}$ >4 = significant difference; <4 = no significant difference
		Febrile Stage		Convalescent Stage		
Disease	No. of Cases	No.	Rate	No.	Rate	
Scarlet fever	854	35	0.041 ± 0.007	179	0.210 ± 0.014	10.88
Measles	283	19	0.067 ± 0.015	50	0.177 ± 0.023	4.04
Diphtheria	140	16	0.114 ± 0.027	27	0.192 ± 0.033	1.83
Miscellaneous diseases	210	12	0.057† ± 0.016	23	0.110 ± 0.022	.....
Total	1,487	82	0.055 ± 0.006	279	0.188 ± 0.010	11.29

* The total number of 1,487 is sufficient to give a stable rate, during both the febrile and the convalescent stage. The rate during the convalescent stage is significantly higher than that during the febrile stage (approximately 70,000,000,000 : 1; i. e., the chances against this being a chance phenomenon are 70,000,000,000 : 1. There is great significance in the difference between the rates in the febrile and convalescent stages of scarlet fever and measles.

† Not a stable rate.

Analysis was made by means of mathematical formulas, and as shown in the table. The formula $\frac{K}{PE_K}$ is explained as follows: K indicates the difference between the rates of reaction in the febrile and convalescent stages, and PE_K indicates the probable error of this difference. When $\frac{K}{PE_K}$ is greater than 4, it is statistically significant. Thus, the result 10.88 indicates that the chances are about 70,000,000,000 : 1 that the difference between the rates of the cutaneous reaction to tuberculin in the acute and the convalescent stages of scarlet fever is not a chance phenomenon. In diphtheria, however, the figure 1.83 is obtained, indicating that chance alone may bring about such a result once in four times without the operation of any causal factor. This is not statistically acceptable proof that there is any real effect of diphtheria on the tuberculin cutaneous reaction.

Tables are shown and a statistical analysis given to demonstrate that the tuberculin reaction may be not only diminished in extent during acute diseases but also delayed.

There is discussion as to whether the amount of tuberculin used in the initial cutaneous test was sufficient to bring about sensitization to tuberculin and thus cause the cutaneous reaction later to become positive or to be increased in size.

Against this possibility is the fact that in certain instances of scarlet fever and measles the tuberculin cutaneous test was positive within a few months before the onset of the acute disease. In about one third of these cases the reaction became negative, but in all it again became positive during convalescence. In addition, the rate of positive reactions obtained during convalescence, when compared by mathematical study with the rate in a group of children tested for the first time, showed no difference, and, furthermore, the size of the reaction was not statistically different in these two groups. Work in progress, however, suggested that the injection of human tubercle bacillus protein may lead subsequently to a small, fleeting reaction, so that it is not proper to state unequivocally that sensitivity to tuberculin may not be brought about.

From a practical clinical standpoint, failure to elicit a cutaneous response to tuberculin during the acute stage of scarlet fever and, probably, of measles cannot be accepted as evidence that the person is a nonreactor. No statistically significant difference can be demonstrated between the rates of positive reactions to tuberculin during the acute and convalescent stages of diphtheria.

DISCUSSION

Dr. James Dowling Trask, New Haven, Conn.: Can changes in the response to the tuberculin test be correlated with the complications and sequelae of scarlet fever?

Dr. A. A. Weech, New York: Is not the severity of the febrile reaction more closely related to the suppression of the tuberculin reaction than the particular disease responsible for the fever?

Dr. Henry J. Gerstenberger, Cleveland: Dr. Pilcher found that there was the same response to intracutaneous injections of codeine as to intracutaneous injections of tuberculin. His conclusion was that the diminished response was due to the change in the vascular system during measles.

Dr. Béla Schick, New York: Dr. Mitchell has proved that during scarlet fever there is a change in the reactivity to tuberculin. So far as measles are concerned, I believe that the cutaneous reaction becomes less intense and is eventually suppressed. Preisich, before von Pirquet, was the first to observe the influence of measles on the reaction. Gruener found that tuberculin reactivity is diminished only, not entirely suppressed. With larger doses of tuberculin, the tuberculin reaction becomes positive. I know from the literature that during the height of whooping cough reduction of the tuberculin reaction has been eventually observed.

Dr. Joseph Stokes Jr., Philadelphia: In a few cases we used some tuberculin which gave no sensitization at all. This material was tried in a few patients with high temperature, particularly in pneumonia. Whereas the tuberculin reaction of this material was slightly positive during the height of the disease it reappeared markedly after the disease had disappeared and the temperature was lower, which fits in well with Dr. Mitchell's results.

Dr. A. Graeme Mitchell, Cincinnati: If faith may be placed in statistical analysis by the methods we have employed, it appears that scarlet fever exerts a more marked effect on the tuberculin reaction than does measles. Measles has been mentioned particularly in the literature as the disease causing suppression of the tuberculin cutaneous reaction. It has been asked whether this depression in cutaneous response is related to the severity of the disease. Affirmative opinions have been stated, but we do not believe that this has been satisfactorily demonstrated. We are not prepared to answer this question, although it is an interesting and proper one, but are now attempting to analyze our figures to see whether the results can be linked up to such a factor as the height of the fever. We have shown that diphtheria does not significantly affect the tuberculin skin reaction, and this disease is usually accompanied by a lower fever than that in scarlet fever or measles. Other diseases not accompanied by high fever do not appear to affect the cutaneous reaction markedly. The

depression of the response is not a local effect of the rash, since depression occurs in diseases such as pneumonia, which are not accompanied by an eruption. It is interesting that, as we reported previously, the Schick test and the Dick test do not appear to be affected in a nonspecific way by diseases other than diphtheria and scarlet fever. It would appear that if a local cutaneous effect only is operative in depressing the tuberculin skin reaction, other tests, such as the Schick and Dick tests, should also be demonstrably affected by these acute diseases.

Second Session

Thursday Evening, May 3

EXPERIMENTAL PRODUCTION OF POLIOMYELITIS IN MACACUS RHESUS MONKEYS. DR. JOHN A. TOOMEY (by invitation), Cleveland.

This paper describes the results obtained when portals of entry other than intracerebral were used to introduce the virus of poliomyelitis into Macacus rhesus monkeys.

Poliomyelitis was produced either by injecting the virus into the lumen of the ileum or by injecting it subserosally in the lumen of the small intestine. Absorption of the virus took place possibly along the nerve fibers of the intestine (the sympathetic system) to the somatic nerves and from there to the cord.

That absorption can take place from the sympathetic system was demonstrated when the disease was produced in the arms of monkeys after intrasciatic injections of the virus, even though the cord had been previously transected in the dorsal area so that the only connection left between the upper and lower part of the cord was by way of the sympathetic nervous system. Likewise, after the cord had been sectioned in the dorsal area and the virus had been injected intracerebrally, virus was found in the lumbar area of the cord, even though there was no connection between the upper and lower part of the cord save by way of the sympathetic system.

When 70 per cent alcohol was injected into the superior mesenteric nerves at the base of the small intestine and along the inferior mesenteric nerve ramifications that supply the large intestine, and then virus was introduced intracerebrally, there was a modification of the disease in 2 experimental monkeys, in that they did not become seriously ill until the twenty-third and twenty-fourth days, respectively, after injection. Two control animals which were given injections of virus alone showed quadriplegia on the sixth and seventh days, respectively, after injection.

EPIDEMIOLOGIC STUDIES IN MEASLES. DR. S. KARELITZ (by invitation) and DR. BÉLA SCHICK, New York.

Experiments were carried out in order to ascertain whether exposure of adults to measles in the stage of catarrhal symptoms (with Koplik spots) increased the protective power of their serum. These experiments were to a certain extent positive, but were not conclusive. It was observed that a difference existed in the protection afforded against measles between children in institutions and those in families. In institutions, in which each patient with measles is isolated as soon as possible, it is easier to protect other children against measles than it is in families. Also, in noninstitutional cases one must differentiate between families in which the patient with measles is immediately isolated and those in which other children remain in contact with the patient. Repeated exposure of children to measles during the first days of the infection has, therefore, a decided influence on the amount of adult serum necessary for their protection against measles. The efficacy of a serum should be evaluated not by its results in children in institutions, but only by those obtained in children living in families where they have been intensively exposed to measles.

DISCUSSION

DR. CHARLES F. MCKHANN, Boston: The determination of the factors influencing the effectiveness of serum against measles is not a simple problem. I agree with Dr. Schick that among other things the degree of exposure must be considered. Physicians have thought in the past that the dosage and potency of the serum in relation to the time of injection were the important items, whether one was dealing with convalescent serum or adult blood. However, the age and size of the patient and the degree of exposure are probably factors. Yet it is difficult to establish their exact importance quantitatively.

For the past ten years the Children's Hospital of Boston has kept statistics on the incidence of measles and chickenpox among nonimmune children exposed in the wards of the hospital. The incidence of the diseases following exposure in the hospital does not parallel that following exposure in the home. In the home, exposure means almost 100 per cent likelihood of infection, particularly in homes with poor hygienic conditions.

In the Children's Hospital, statistics covering the incidence of measles following exposure in a ward cannot be used, because we employed serum freely to

Results of Use of Placental Extract in the Prevention and Modification of Measles to April 17, 1934

		Protection	Modification	Failure
Crude Material				
At home				
To protect	15	11	4	0
To modify	3	0	3	0
In institutions				
To protect	100	98	2	0
To modify	0	0	0	0
Refined Material (various fractions)				
At home				
To protect	71	53	13	5
To modify	119	62	53	4
In institutions				
To protect	216	188	15	13
To modify	4	1	2	1
Total	528			23

control the disease. However, in chickenpox, for which serum has not been used, only about 35 per cent of the nonimmune children theoretically exposed contract the disease following contact with a single case. These figures may be used as control data with reference to measles, as the communicability of the two diseases is nearly equal. Thus, if one had 15 nonimmune children in a hospital ward to whom one gave measles serum for prophylaxis following exposure to the disease, and if 5 of the children contracted measles, complete failure of serum protection would have to be presumed, because without serum protection only 5 of the children would have contracted measles following this degree of exposure.

So in a statistical analysis of the effectiveness of serum there is no doubt that the degree of exposure is an important item, and if one analyzes statistics regarding the efficacy of serum, I agree with Dr. Schick that it should be known whether the exposure to the disease was in the home, at school or in a hospital and how long contact continued.

It might be interesting to present data regarding the use of placental extract, about which I talked last year, to show how it bears out what Dr. Schick has stated. In our statistics in the past year we separated patients exposed in institutions and homes. Cases due to contact at school, in hospitals or among playmates constitute one group and those due to exposure in the home to a brother or sister with the disease the other. In all, we had 528 opportunities to use placental extract in nonimmune patients exposed to measles. In this series there were 23 failures.

The more we have attempted to refine the material and reduce it to the active principles, the more failures there have been.

While I am not prepared to substantiate entirely Dr. Schick's statement that one has to increase the dosage of serum for patients who have been more thoroughly exposed to the disease, I am certain that one must weigh carefully the various factors that influence the number of persons infected in the homes or in hospitals, when analyzing statistics regarding the effectiveness of serum.

DR. THOMAS MILTON RIVERS, New York: Theoretically, the convalescent serum should not be effective in the amounts used. The reason for this is the extent of dilution that the serum undergoes when it is injected. When neutralization tests are performed it has been observed by many workers that dilution of the serum to any great extent inactivates its neutralizing properties. Therefore, if the convalescent serum used as prophylaxis in human beings works in the same manner as it does in neutralization tests, much larger amounts should be necessary to obtain the results reported by many clinicians. Physicians know that the serums are effective, but they do not know how they act. I wish that the clinicians who are using the convalescent serums would try to give an idea of why they are effective.

DR. BÉLA SCHICK, New York: Dr. Rivers has given his explanation of the efficacy of measles serum, a difficult theoretical problem. In test tube experiments, such a dilution of serum as occurs by injection would interfere with the restriction of the veins; clinically, the serum undoubtedly is effective.

The difference between results in home and hospital practice is important. One should not be satisfied with judging the results of a given serum on the basis of experience with hospital patients. I observed from our study that frequent reexposure on the first day of incubation may influence the intensity of the disease, which is to be expected. One may expect similar effects of reexposure in other diseases with a long incubation period. For instance, in tuberculosis there is more time for reexposure. It must make a difference whether a child is exposed only once in a short contact to a person with tuberculosis or whether he is exposed repeatedly several days in succession.

LIPOIDS AND LIPOID DISEASES: IV. THE LIPOID CONTENT OF THE TISSUES IN STATUS EPILEPTICUS, TOXIC ENCEPHALOPATHY AND CHRONIC LEPTOMENINGITIS. DR. D. MURRAY COWIE and M. CATHERINE MAGEE, M.S. (by invitation), Ann Arbor, Mich.

McQuarrie and his associates demonstrated clearly that the phospholipoid-cholesterol quotient of the blood of an epileptic person during an epileptic attack is higher than at any other time, thus definitely establishing a relationship of the blood lipoids to status epilepticus. They point out that this relationship obtains whether the cholesterol content of the blood is high or low.

In August 1932, an opportunity to determine the lipoid content of the tissues of an epileptic child dying in status epilepticus presented itself. A higher phospholipoid-cholesterol quotient was found for the tissues of this child than could be demonstrated for the tissues of a patient dying of Schüller-Christian's disease and another patient dying of severe anemia. Since I was unable to find any analyses of the tissues of children in the literature, and since the patients mentioned were much younger (2 years and 10 months of age) than the patient whose case we are now recording, we determined the lipoid content of the tissues of children of approximately the same age dying from other causes, for the purpose of comparison. In each of these the central nervous system was involved.

This study showed that in the case of epilepsy during status epilepticus the phospholipoid-cholesterol quotient of the liver, the spleen and particularly the skeletal muscle tissue was markedly higher than that of tissues of children dying from the other conditions observed. It was definitely higher in the lung tissue. The same situation obtains in the tissues as has been shown to exist in the blood of children during an epileptic attack.

OSTEOMYELITIS IN CHILDREN. DR. SAMUEL AMBERG and DR. R. K. GHORMLEY (by invitation), Rochester, Minn.

Close cooperation of the pediatrician and the orthopedic surgeon is necessary in the treatment of most patients with osteomyelitis. There are not sufficient statistical data with regard to the outcome of the disease or the effect of various procedures.

It is dangerous to generalize from illustrative cases, and often not sufficient time is allowed to determine the final result. Including patients with infection of the bones of the head and excluding those with mastoiditis and its sequelae, 394 patients with osteomyelitis have been seen within about twelve years in the Mayo Clinic.

The distribution as to age, sex and single and multiple osseous involvement is given. The rôle of injury and infection in the etiology of the disease is discussed, and attention is called to the fact-finding work of Lexer, published thirty-eight years ago.

The relatively mild cases and the 4 fatal ones studied are discussed. No fatalities occurred among patients in the first year of life. One patient died in shock, and 5 died after leaving Rochester. Other fatalities may have occurred. One of the patients died from acute leukemia.

The mortality from osteomyelitis was 2.8 per cent. Statistics on the mortality in this disease appear to be rare. Attention is called to the nonoperative cases.

Some nonsurgical features are discussed, such as the infrequency of original glandular and splenic enlargement and the incidence of anemia, leukocytosis and symptoms of disorders of the urinary apparatus (pyelonephritis, bacteriuria) and blood cultures.

The incidence of lengthening or shortening of the extremity and of more or less disabling changes in the joints is given. Attention is called to the protracted cases as well as to the so-called recurrent ones. It is shown that the chance for healing is better in patients with involvement of a single bone than in those with multiple osseous involvement. It was surprising that the patients who had had surgical attention during the first three weeks did not do much better than those operated on later, but it is emphasized that further studies may present an entirely different picture.

Some cases are reported to demonstrate the difficulties confronting the pediatrician and the necessity of close cooperation with the surgeon. The surgical treatment is discussed.

DISCUSSION

DR. H. W. HUDSON JR., Boston (by invitation): In giving some impressions from the surgical and orthopedic services of the Boston Children's Hospital, confined to osteomyelitis in patients under the age of 2 years, I should like to emphasize the fact that time taken in making a diagnosis and in medical treatment, if by the latter one means nonoperative treatment, is of great importance in this age group. It is seldom of great importance than an operation be immediately performed.

Differential diagnosis may be difficult at times but observation over a period of several days does no harm to the child and gives an opportunity for a more accurate diagnosis.

In addition, it seems to some of us, at least, in the hospital that the treatment of the patient rather than the treatment of the bone or bones which may be involved is of the greatest importance.

In children of this age group the problem of osteomyelitis has to be split off from the general problem, since almost invariably the infection starts adjacent to the epiphyseal-diaphyseal line and is often limited to that, breaking through the periosteum early, resulting in a soft tissue abscess which may be drained as well after several days, when the systemic condition is better than earlier.

It is our impression that the prognosis for the bones of these children is good, provided that the child recovers from the infection.

Dr. Amberg has suggested that the statistics are difficult to interpret, and they are. I should like to cite statistics soon to be published by Green and Shannon,

from the Children's Hospital, including those regarding a group of 95 patients under 2 years of age with osteomyelitis. These figures show an uncorrected gross mortality of 21 per cent, a mortality of 43 per cent under the age of 6 months and a mortality of 41 per cent over the age of 6 months. The study covers a period of twenty-one years.

A series of 34 cases occurring in the last three and one-half years gives somewhat different figures. At the Children's Hospital, patients with osteomyelitis are distributed equally between the surgical and orthopedic services, with the exception that the surgical service is more apt to receive the patients with lesions or infections elsewhere than in a single bone. In the orthopedic service within the past three and one-half years, 20 consecutive patients with this disease were treated, with 1 death—a mortality of 5 per cent. In the surgical service there were 14 patients with 3 deaths. That gives for the group of 34 cases a mortality of approximately 10 per cent.

The possibility should be borne in mind that when these patients are well treated systematically they may not need an operation. Frequently one has seen patients presenting all the clinical evidence of osteomyelitis, with later evidence by roentgen examination, who recovered without operation and whose bones at a remote follow-up period appeared to be normal.

Dr. Samuel Amberg, Rochester, Minn.: Dr. Hudson has presented an interesting discussion. It is surprising that of our 16 patients seen during the first year of life none has died.

One of the points which I should like to emphasize again is that for some reason or other we do not have good statistics with regard to the surgical treatment of this condition. It is interesting to hear that these statistics are to be supplied.

So far as I have been able to judge, some illustrative cases have usually been presented, after which one is led to believe that other cases behave likewise. They may not do so. This subject needs to be treated statistically.

Third Session

Friday Morning, May 4

Reduction of Neonatal Mortality in the Premature Infant. Dr. Stewart H. Clifford (by invitation), Boston.

The pediatric service at the Boston Lying-in Hospital during the past few years has extended its field of interest to include a study of the fetus in utero, with particular reference to estimating its weight and the effect of various obstetric factors on its viability. As a result of these investigations the pediatrician has been able to be of practical assistance to the obstetrician in a more successful management of certain types of premature labor.

A roentgen technic for mensuration of the fetal head in utero has been perfected, so that the occipitofrontal diameter can be predicted with accuracy. The relation between the occipitofrontal diameter and the weight at birth has been established by actual measurements in more than 600 new-born infants. From the diameter of the head obtained by roentgenograms it is possible to give a reliable prediction as to the probable and minimum weight of the fetus in utero. Under certain circumstances, when the fetus is found to be small and when the condition of the mother permits, artificial induction of labor or delivery by cesarean section may be postponed until a more viable baby can be assured.

A statistical study has been made of 958 consecutive deliveries of premature infants in order to determine the influence of maternal complications of pregnancy, methods of delivery and the administration of morphine during labor on the fate of the child. The information thus accumulated enables the obstetrician to elect the safest method for the delivery of the individual infant which is consistent with the well-being of the mother.

DISCUSSION

DR. ETHEL C. DUNHAM, New Haven, Conn.: I desire to congratulate Dr. Clifford on the fine presentation of his material. His conclusions are interesting. This paper gives great hope of bringing about a reduction in mortality in the neonatal period.

As I pointed out last year at the meeting of this Society, the decrease in neonatal mortality has been slight within the last ten years. There seems to have been an attitude among some pediatricians that one could not reduce this mortality much lower. I believe that this is a wrong point of view. All the figures, without exception, show that prematurity plays by far the greatest rôle in neonatal mortality. Any contribution to the understanding of the causes of death of premature infants is of importance in helping to solve the problem of reducing this mortality.

Dr. Clifford's work has brought out a number of important ways in which this mortality can be reduced. I also found in an analysis of neonatal deaths that morphine given to the mother during labor played an important rôle in neonatal and fetal mortality. I wish to add that, in analyzing the causes of infant mortality following cesarean section, I have come to believe that not only the morphine given to the mother but also the method of resuscitation of the infant is important in cases in which the section is done before the onset of labor. The changes in the carbon dioxide and oxygen content of the infant's blood which take place normally during labor have not taken place when delivery was by section before labor began. There is reason, therefore, to suppose that the methods used for resuscitation of the infant born by cesarean section should be different from those used when the infant is born after a normal labor. I wonder whether Dr. Clifford divided the infants delivered by cesarean section into those delivered before and those delivered after the onset of labor?

DR. HENRY L. K. SHAW, Albany, N. Y.: For those members who live in small cities the question of where the work of the obstetrician ends and that of the pediatrician begins is an interesting one. The obstetrician takes exclusive care of the baby for from one month to one year, and often the pediatrician does not see the child until it walks into his office. Therefore the pediatrician cannot be blamed for the high neonatal mortality.

As Dr. Talbot has said, the mortality of infants past 1 month of age has been reduced almost to the minimum, while there has been little reduction in that of infants in the first month of life. In New York State, 65 per cent of the deaths in children under 12 months of age occur in infants less than 1 month old, and in about one half of these within the first twenty-four hours. In New York City the Academy of Medicine prepared an exhaustive study on maternal mortality. This has aroused a great deal of interest among both the laity and physicians. No reference was made in this report to neonatal mortality. This is a subject in which the American Pediatric Society could make a valuable contribution. In the past the problems of scurvy and vulvovaginitis were exhaustively studied by special committees. Could not neonatal mortality be likewise investigated?

DR. LAWRENCE T. ROYSTER, University, Va.: I compliment Dr. Clifford on this interesting study. It points clearly to the fact that cooperation between the obstetrician and the pediatrician is necessary. I wish to point out one thing only: Modern methods have lessened the mortality to some extent, but one cannot stress too strongly the advantage of a more general use of episiotomy in the delivery of premature infants.

DR. JULIUS H. HESS, Chicago: I have a few figures which emphasize everything that Dr. Clifford has said. In our station for premature infants we have had 999 infants weighing less than 2,000 Gm. Of those, only 77 weighed less than 1,000 Gm. This must be only a small percentage of such infants born. In other words, our station is independent of an obstetrical hospital and the patients come in from various sources. Of the 77 infants who weighed less than 1,000 Gm., 12, or 15.5 per cent, were graduated. In the entire group there were 316 weighing between 1,000 and 1,500 Gm.; of these, 137, or 43.3 per cent, were graduated. There were 606 weighing between 1,500 and 2,000 Gm.; of these, 456, or 75.2 per

cent, were graduated. Only a small percentage of those weighing less than 1,000 Gm. and a limited number of those weighing less than 1,500 Gm. ever reach a hospital. This speaks decidedly for the desirability of prolonging intra-uterine life.

What has been said about morphine anesthesia, also what Dr. Dunham has said about the necessity of being prepared to resuscitate the patient with either oxygen or a combination of oxygen and acid gas, applies to our cases.

DR. A. A. WEECH, New York: It is generally stated that embryonic tissue is peculiarly susceptible to irritation by the roentgen rays. For this reason obstetricians are frequently unwilling to employ the roentgen rays for diagnostic purposes. I presume, from the large number of roentgenograms in this series, that Dr. Clifford is able to offer reassurance on this point. I should appreciate a word from him concerning the harmlessness of the procedure, if it is harmless.

DR. F. C. RODDA, Minneapolis: In Minneapolis, in spite of the finest cooperation with our obstetric confrères, we, too, have met with a discouragingly high mortality in babies delivered by cesarean section, even when the operation has been speedily and skilfully performed.

Dr. Scammon has called attention to the large amount of blood in the placenta at the moment of delivery. Rightly, the obstetrician wishes to complete his work speedily. Immediately on delivery the cord is clamped, and little time is permitted for the blood to pass from the placenta. Frequently in such cases the baby goes into collapse and presents sunken fontanels. I believe that if a little time were permitted for the blood to pass to the infant one would find a sharp drop in the mortality of babies delivered by cesarean section.

DR. LOUIS C. SCHROEDER, New York: In certain sections of the country there are increasing numbers of deliveries by cesarean section performed under spinal anesthesia. I wonder whether any of Dr. Clifford's series were performed by this method. If there were such a series, it would be of interest to classify the results according to the type of cesarean section performed and the method of anesthesia employed.

DR. STEWART H. CLIFFORD, Boston: To arrive at the explanation of the detrimental effect of cesarean section on premature babies will require many years of work and investigation, particularly along physiologic lines. The fact remains that premature babies do die after delivery by the method which should be most ideal.

It is our impression that it is the technic of the cesarean section that is at fault. It may be that the cord should be permitted to stop pulsating before it is clamped and cut, as has been suggested. It may be that one will have to speed up the operation from the time of the first drop of anesthetic until the baby is delivered. It may also be that the type of anesthetic will have to be changed. Theoretically, spinal anesthesia should be ideal in eliminating the possibility of an anesthetized premature infant, but in practice it has failed to improve the condition of the infant delivered by cesarean section. During the past year particular attention has been paid to cesarean delivery of premature infants, and most of these deliveries have been performed with local anesthesia preceded by oral administration of pentobarbital sodium. The mortality was higher under this régime than during the preceding year, indicating that the problem remains unsolved.

Something happens when the weight of the infant passes 5 pounds (2,268 Gm.); the mortality of infants heavier than this, when delivered by section, is practically zero.

In answer to Dr. Dunham's question, our series was originally divided according to the type of cesarean section: the classic or the Kerr technic. When we analyzed the results statistically, no significant difference was discovered. The results by the two methods were therefore considered as a whole so that we could base our statistics on as large a group as possible. In regard to Dr. Dunham's second question most of the mothers were not in labor when section was performed.

Our experience is in agreement with Dr. Royster's. I should have mentioned that low forceps delivery with wide episiotomy is performed. This seems to reduce

the trauma to the fetal head and to contribute to the low mortality associated with this procedure.

As to the possible detrimental effect on the fetus of exposure to the roentgen rays, before we began our study we were assured by workers in several obstetric centers that the dosage used would be safe for the fetus. We have taken more than 600 roentgenograms of the fetus in utero, 250 of which were taken last year, and as yet have observed no ill effects. In some of our studies we tried to determine the rate of growth of the individual head, beginning about the fifth month, or as soon as it is demonstrable by the roentgen rays, and measuring every four to six weeks until birth. In spite of these repeated exposures, we saw no ill results.

It may be of interest that during the coming year an intensive study of toxemia is to be undertaken. In this investigation the internist, the cardiologist, the obstetrician, the chemist and the pediatrician plan to gather around the individual patients in order to determine the most successful means of handling situations from the standpoint of both mother and fetus.

During the past two years a pleasant part of our work has been helping the obstetrician, not only through prediction of fetal weights, but also in discussing the safest methods of managing matters in the light of the maternal complications and size of the fetus.

Roentgen measurement of the size of the fetal head is accomplished by means of a stereoscopic technic that was described by McKenzie Davidson in 1899 and independently worked out by Clayton R. Johnson of California. The method was described in detail in the April 1934 issue of *Surgery, Gynecology and Obstetrics.* It is very simple; any machine capable of taking stereoscopic pictures, with a lateral shift, which can be adapted at little expense, suffices. We first take two stereoscopic pictures of the fetal head in utero. The distance from the tube to the film is known, as is the distance of the tube shift. By means of a dummy we reproduce the conditions under which the rays from the tube register on the original picture. Beginning at the film, we retrace the path of the rays to its source at the target. By means of this reconstruction the size of any object included on the exposed film can be determined by direct measurement. In every examination we place two 10 cm. metal bars on the patient's abdomen to act as controls. These rods are first measured, and if these determinations prove correct, it is assumed that those of the occipitofrontal size are also accurate.

STANDARDS OF REFERENCE FOR PHYSICAL DEVELOPMENT, SUGGESTIONS FOR PRESENTATION WITH AND USE IN CLINICAL APPRAISEMENT. DR. HAROLD C. STUART, Boston.

This paper deals with methods of applying measurements of children in an attempt to improve clinical judgments regarding their physical development. It indicates the kind of information which is sought, the limitations of most norms and modifications in their presentation and use which should increase their practical utility. The relative value of particular measurements and the use of measurements in research are not considered.

A simple method of assembling and presenting in reasonably comparable form data obtained through different procedures is needed. To have measurements fit into this comprehensive picture satisfactorily is necessary, and the opportunity of making direct comparisons between objective and subjective data seems desirable. Measurements should reenforce and improve clinical judgment, rather than displace it. The presentation should not minimize the attention paid to figures, but should rather emphasize the significance of the latter.

The concept of the usual range or distribution of physical attributes is an important one, and it is desirable to compare each attribute of the child under examination with this distribution, rather than with an average or any other single norm. It is not only desirable to compare relative position in the distribution of one measurement with that of another and with various clinical judgments at

a given time, but there should also be an opportunity to compare position at one time with that at another, so as to note relative progress.

The expression of all measurements in percentiles of the usual distribution favors this kind of analysis, and such expressions are more readily grasped and visualized than are means and sigmas or other statistical methods. Exactness is not a requirement for this purpose, for general position only in the distribution scale is the information to be arrived at.

The percentile distributions of measurements taken in the study of growth at the Harvard School of Public Health for age intervals during the first two years are presented. These tables are offered as examples of the kind of material which seems to be needed. The measurements were selected for this age period only, and others should supplement them in the study of older children. One of the advantages of this method of presentation is that the measurements used may vary from period to period, without destroying the opportunity for direct comparison. Although these tables are not based on adequate numbers to be used as ultimate standards and although they deal only with northern white persons of a limited social range, they may be used for clinical comparison at these ages. They allow for the direct placement of any measurement in one of six categories within the distribution, as well as above or below it. The actual percentile on which the measurement falls may be obtained by plotting the norms against a scale of 100, but such detailed consideration adds little to the value of the interpretation. Sample charts are also presented to suggest the practical use of this material with individual children. In addition, a few examples of cases are shown with lantern slides.

The limitations on the practical usefulness of measurements are recognized, both because of technical inaccuracies and because of difficulties in determining their significance. The number of measurements which can be taken with profit is small, particularly during the years covered by the tables. I believe, however, that the attempt to secure and interpret a few simple measurements improves clinical judgment and brings to one's attention physical characteristics which would otherwise be overlooked. Their usefulness is, in a large measure, dependent on the way in which they are analyzed and interpreted.

DISCUSSION

Dr. Alfred H. Washburn, Denver: I desire to compliment Dr. Stuart on this excellent paper and presentation. Some of the members who have recently become intensely interested in the study of growth and development appreciate the tremendous amount of work that has gone into this paper. We also appreciate the value of such work in clinical pediatrics.

It is obvious that if one is to diagnose disease early one must acquire definite information as to where health ends and the pathologic process begins. In order to do so, one must study the individual variations of different children within the realm of health and the variations in any one person from time to time.

One of the greatest difficulties encountered in making this sort of pediatric study has been the lack of any method. There is no clear outline of a method of procedure in carrying out such a study. One searches the literature and finds little help. One has to work out methods. Dr. Stuart is making an important start in working out methods for some of these studies.

In regard to method, there is always danger in taking method at any one time too seriously; I know that Dr. Stuart will agree with me in this.

Sir James Mackenzie once said that the practitioner could make some of the most fundamental contributions to the study of the individual human being and his life cycle by depicting the individual variations with which one must be familiar before one can say where health ends and pathologic processes begin. He was interested in this problem and was one of the first to outline the necessity for the study of the life cycle of man.

Those who, like Dr. Stuart and myself, are in this sort of work find themselves up against this proposition: A child is studied with great thoroughness, a method is worked out as fully as possible, the findings are tabulated and analyzed so

far as it is possible. The data may appear to be within the realm of health. One may then consider the child's clinical appearance and know that he is not healthy. One has not worked out sufficiently the method for picking out abnormality in terms of objective data.

May I make a plea that those who are in practice try to reduce observations to objective terms and hand on to those who are studying the child more and more data as to what objective means can be used for checking on what sort of person a child may be.

DR. HAROLD C. STUART, Boston: I appreciate Dr. Washburn's remarks in regard to method. Method is unimportant, except as it influences thinking. It seems to me that thinking about measurements is much befogged at present.

I have had the impression that there are two types of pediatricians: those who do not use measurements, but who make evaluations on the basis of what they see, and those who take a series of measurements and arrive at decisions in the same manner as the first group, ignoring the measurements taken. For my own satisfaction, I wanted to find some method of using measurements so that they would mean something to me. Perhaps the method I should find useful would be of no value to any one else. I simply suggest this approach as one way of interpreting measurements so as to bring out their meaning.

CHILD HEALTH RECOVERY PROGRAM. DR. MARTHA M. ELIOT, New Haven, Conn.

The Child Health Recovery Program initiated by the conference called by the Secretary of Labor last October in Washington was undertaken to stimulate interest in the problems of child health that had arisen out of the economic depression and to make sure that the health needs of children should not be overlooked while plans were being formulated to bring about economic recovery. To strengthen and build up child health services throughout the country was clearly one of the major needs.

At the time of the conference there were, according to a census taken by the Federal Emergency Relief Administration for October, 5,184,272 children under 16 years of age in the families receiving public relief; of these, 233,822 were infants and 1,589,480 were children from 1 to 5 years of age.

Previous to the calling of the conference there were many indications that the health and nutritional condition of children were being adversely affected by the economic depression and that the amount of medical care being given was decreasing. Recent reports by G. H. Berry from the Association for Improving the Condition of the Poor in New York City and by Perrott, Collins and Sydenstricker and C. E. Palmer of the United States Public Health Service verify these earlier impressions. Furthermore, there is evidence that appropriations for child health activities have been materially reduced in many communities. Recent reports from the state health officers indicate that during 1933 and 1934 appropriations for state child health activities have been wiped out in four states and reduced in thirty-three others. There has been no change in appropriation in only two states, and there has been a net increase in only four. Altogether, nine states have no appropriation in 1934 for child health work. Eight have less than $5,000; six have from $5,000 to $10,000 and twenty-five have $10,000 or more. Only twenty-two states have a full-time physician in charge of child health activities.

The Child Health Recovery Program had as its objectives: (1) the location of undernourished children; (2) the development of ways and means of overcoming existing malnutrition and preventing its further progress through dietary measures, and, so far as necessary, the institution of corrective medical procedures. With the aid of nurses employed under the Civil Works Administration, programs have been undertaken in approximately forty states. These programs have varied according to the needs of the state and the facilities for organizing and carrying out a given plan, but in most instances a program centering around the nutritional needs of children has been developed. In a few states programs for immunization against diphtheria have been the chief activity. In a number of states joint

action on the part of the state health department and state medical, pediatric, dental and nursing associations, together with the state relief administrations and other interested groups, has resulted in well organized programs for child health, which may have permanent value. The organization of local committees in counties or smaller communities has been a factor in influencing local public opinion in favor of a permanent program. Details of accomplishments cannot be given, but already reports have come in to the Children's Bureau that many examinations have been made, many school lunches given and a considerable number of abnormal physical conditions corrected. Consultations by the nurses with local relief administrators have resulted in more adequate relief in many instances. The cooperation of nutritionists and extension workers has been sought, and state-wide school feeding programs have been organized, in a number of states. Deliberate effort has been made to focus attention on the nutritional needs of children, both those in families on relief and those in families who, though not on relief, are in need because of unemployment. The need of joint planning and joint activity on the part of health departments and medical groups, especially the pediatricians, in the organization and carrying out of a state child health program has again been emphasized.

DISCUSSION

DR. GEORGE M. LYON, Huntington, W. Va.: One's appraisal of any program of this type depends largely on the point of view one takes in the beginning. In discussing the results of the program that has been carried out in West Virginia it is probably worth while to say something about the background which our state presented at the beginning.

West Virginia has many of the stranded industrial mining communities that constitute a serious problem at present. It also has one of the highest death rates of the states in the Union, particularly as regards children under 2 years of age. In the fifty-five counties there are only thirteen full-time county health units, not one of which would be considered by Dr. Eliot's criteria as an acceptable full-time public health unit.

The state had, throughout the winter, about 30 per cent of its families on the relief roll. From that standpoint it was the leading state in the Union. The State Department of Public Health has an annual appropriation of about $90,000, which is grossly inadequate. The division for Crippled Children of the Department of Public Welfare has an appropriation of $95,000 a year; so the program for crippled children has actually obstructed the program of general child welfare and public health in the state. No outside money has come into the state for the purpose of aiding any health activity, except from the Rockefeller Foundation. The Commonwealth Fund has gone into other states and has been used for demonstrations, but West Virginia has not had anything of that sort. The first opportunity the state had had to do something of that kind was afforded by the emergency relief program. The physicians of the state were glad of the opportunity and availed themselves of it.

Instead of the Director of Health and Nutrition working only and directly through the Department of Public Health, the program was carried on through the medical society as a whole and the pediatricians of the state in particular. It has worked out fairly satisfactorily. The State Administrator was also the director of the Department of Public Welfare and appointed as Director of Health and Nutrition an efficient person by the name of Mrs. Trent, who knew the state and its peculiarities. She has been able to do the work in a splendid manner. The secret of her success was that she went directly to the organized profession instead of working through the Department of Public Health.

The pediatricians thought that too much emphasis on weighing and hurried examinations was unwise. We tried to avoid conclusions about how much "health recovery" we were carrying on. We believed that food relief was the prime essential, and the children got that. Seven and one-half cents was allowed workers for individual meals. The first lists of menus submitted provided approximately 350 calories. That did not seem adequate from the standpoint of hungry children. We insisted on 850 or 900 calories, even if beans or corn bread and

molasses had to be included in the diet. The problem of getting calories in food seemed more important than any constructive educational program. One cannot carry on an effectual educational program on 7½ cents a meal, when this meal provides the bulk of the food taken in that day. We tried to discourage the workers from drawing conclusions from the weights of the children before and after the program was put into practice, as we thought that this was not a constructive feature.

The health educational part of the program was probably the most outstanding feature. In five counties in West Virginia rather elaborate health educational programs have been carried out, based somewhat on the fundamental principles advocated by Vaughan in Detroit in regard to medical participation in public health.

I have in my hand the material gathered from one of the counties at the expense of the recovery program. It is educational for the teachers and for the physicians. It is a large project in adult education and begins first with the physicians and then with the teachers.

Throughout, the characteristic feature of the program has been the large amount of medical participation, rather than participation of any set or special organization, such as the Department of Public Welfare or the Department of Public Health.

We believe that certain projects have been eminently successful and will be influential in molding the public opinion of the state to ideas of better health in the future.

One outstanding thing which the program has done in West Virginia has been to make people aware of the importance of health advice. I believe that in this way it is going to render a permanent good for the state, and that the whole program has been justifiable.

Dr. J. H. Mason Knox Jr., Baltimore: Maryland has been fairly well organized from the standpoint of public health. Every one of the twenty-three counties has a full-time public health officer, with one or more public health nurses. Through the recovery program the state was able to employ seventy-five additional nurses. About 10 per cent of these were public health nurses; the others were all registered nurses, but without much experience in public health.

The fact that the counties were already organized enabled the state to distribute these nurses according to the population and needs under the direction of the county health officers working with the regularly employed nurses. I have just gone over the work. I do not have the figures here, but there was an enormous amount of additional public health work done through this added corps of nurses in the prepartum supervision of mothers, the supervision of infants and preschool children and the nutritional work among, and examination of, school children. Of course, the health officers now feel "let down" a little because of the cessation of the program, but I am sure that a number of projects of great permanent use to the state are now going on because at the time of the economic crisis the state had this important additional help.

Dr. Martha M. Eliot, New Haven, Conn.: I wish to reiterate the fact that the programs in all the states have been different, because of the great diversity of conditions in the individual states.

As a rule, the Child Health Recovery Program has attempted to bring medical, health and relief groups together. The state which Dr. Lyon represents—West Virginia—is one of four or five in which the relief administration or the department of public welfare has had to take the lead. In a number of states the medical societies have cooperated well; in others it has been more difficult to interest medical groups in a child health program.

The Pediatrician and the Rural Child Health Program. Dr. J. H. Mason Knox Jr., Baltimore.

Sir Arthur Newsholme stated that "the health and therefore the hygienic and medical care of every person in a community is a matter of concern and responsibility not only for himself but also to every other person in the same community."

In matters pertaining to health each community naturally turns to its physicians for leadership. As the cost of medical consultation and care in illness is beyond the means of a large proportion of the population of the country, some plan must be established for making preventive and curative measures available to those who cannot provide them for themselves. Among the forms of medical service which have been found helpful in child hygiene may be mentioned: adequate care of mothers before, during and after delivery, consultations in regard to the health of the infant, visits of the child up to school age to the physician and medical supervision in the schools. It is well known that at present these services, especially in the rural areas, are not available to all mothers and children.

The pediatrician can speak with most authority on the value of periodic supervision of the health of the infant and child, for he has been exercising such supervision over his private patients for years, and he knows that those so supervised rarely succumb to preventable disease. It should be a part of the pediatrician's duty to foster a community-wide program of child hygiene in his territory. He may not devote a large proportion of his own time to the project, but from the knowledge which comes from personal experience he can do much to bring preventive pediatrics within the reach of all.

One can rest assured that unless a comprehensive program envisaging preventive care for every child emerges under medical leadership in this country, it will become a demand of popular or autocratic government. Rumbles of the activities in the interest of child health in Soviet Russia are becoming audible.

Twelve Years' Experience in Collecting and Distributing Human Milk.

Dr. Henry D. Chapin, New York.

The Mother's Milk Bureau of the Children's Welfare Federation of New York has collected and distributed 27,526 quarts of mother's milk during the past twelve years. The donors have represented fourteen nationalities—on a city-wide basis.

All donors are required to pass a Wassermann test and a sputum test, together with a physical examination of the heart, lungs, throat, teeth and skin.

The milk is pasteurized, unless the physician orders otherwise. Formerly frequent assays of the milk showed constant ingredients, but some recent assays have shown a tendency to lower fat and protein content, evidently the result of an inadequate diet because of reduced budgets. I question whether the conditions of the mother's endocrine glands do not influence the development of the infant. Premature and very atrophic infants have been especially benefited by this milk; 50 per cent of the recipients have been premature infants; among these the mortality was 15 per cent.

DISCUSSION

Dr. Charles Hendee Smith, New York: I should like to testify to the splendid work of Dr. Chapin in New York City. The Children's Service at Bellevue Hospital has purchased from this agency a certain amount of milk. The hospital has herein a fine working arrangement. The city agrees to pay a certain price for a pint of milk, but at the end of the day, by a sort of "residual legatee" arrangement, the hospital has received what was left over, often much more than twice the amount for which it has paid.

With a fluctuating population of premature infants it is necessary to have an elastic arrangement; that is, each infant has a formula prescribed and ready; the breast milk available is divided among those who need it most, according to the amount available each day.

I think that it is possible to do this in private practice, and I have an idea that it is done more or less in the way in which it was done in the case of a patient of mine many years ago. I had one wealthy patient who had no milk and a patient in moderate circumstances who had a great deal. I organized myself into a distributing agency and fed the premature baby of the wealthy patient by collecting the milk of the patient in moderate circumstances each day, enabling the latter to keep her nurse two or three weeks longer and saving the premature baby's life.

DR. FRANK C. NEFF, Kansas City, Mo.: The collection of human milk through well managed central agencies has been limited chiefly to a few of the largest cities, such as New York, Boston and Detroit. At least these are the ones that we have heard most about. It seems to me that Dr. Chapin might well advocate the extension of this method to smaller communities. There is scarcely a hospital in the country that does general work that could not conduct a small wet-nursing service. This subject as concerning one of the methods of infant feeding should be included in the curriculum of the medical school.

DR. CLIFFORD G. GRULEE, Chicago: During the past few years there has been a general tendency to regard artificial feeding as having reached the point where it is equal to breast feeding, and physicians have consequently taken the position that they are perfectly fortified so far as the infant is concerned.

I have been skeptical about this attitude. Recently the Infant Welfare Society of Chicago made a survey of some 20,000 infants. I shall not anticipate the paper which I shall read before the American Medical Association this year, except to state that the statistics are somewhat as follows:

Infants fed entirely on breast milk constituted about 43 per cent of the group. An almost equal number were partially breast fed and partially artificially fed. The incidence of infection ranged regularly lowest in the breast fed and highest in the artificially fed infants, with that in the babies given complementary artificial feeding in between. What was much more striking was that while only 8 per cent were totally artificially fed two thirds of the deaths in the 20,000 infants occurred in that group. In other words, it seems to me that breast feeding must be promoted if we are seriously to reduce infant mortality after the first few weeks of life. Also, the criterion of successful feeding of infants is not only the nutritional condition of the child but the resistance of the child to infection.

DR. ISAAC A. ABT, Chicago: It will not be out of place to express briefly the appreciation of all the members to Doctor Chapin for coming here to deliver this splendid address. All of us enjoy his continued enthusiasm and interest. There is no physician, certainly none whom I know of, who has contributed so much as a pioneer in social service and social reform in the care of infants and children.

In regard to the use of breast milk in private or hospital practice, all of us see babies who are desperately ill or premature, in whom recovery occurs only when breast milk is supplied.

I wish to thank Dr. Chapin for his interesting and stimulating address.

DR. WARREN R. SISSON, Boston: Dr. Talbot and Mrs. Talbot have sponsored the breast milk industry in Boston. A system has been developed there which now works very well indeed. All the milk ordered from any great distance is sent by express in frozen form. We believe that freezing the milk and dispensing it in that form has solved a great problem for our wet nurses' directory. It has also solved the problem of the preservation of milk which could not be dispensed at the time of collection.

DR. F. B. TALBOT: It is gratifying to have this movement spread as it has. There are now six directories, or whatever one may care to call them, in the country. Milk has been sent by airplane daily to Hartford, northern New York State, Vermont, New Hampshire and Maine. At one time there was a demand for it abroad. The great problem that such directories have had has been to balance demand and supply.

Dr. Emerson now has a satisfactory method of preserving human milk. That is important, because the supply often is much greater than the demand, and sometimes the demand is greater than the supply and is met with difficulty.

For the benefit of any one who may be interested in fostering this movement in some other city, I should like to say that in Boston the directory for mother's milk is the one charity in the city which without any difficulty raised enough money to do more than everything it planned. It is the only charity which received from the drive more than it wanted. All the others got only about 65 per cent of what they asked for.

I believe that Dr. Blackfan has his third year students in the medical school go to the directory and receive an hour or more of instruction in what can be done with human milk. The directory also offers lectures to nurses and public health workers. The directory staff believe that it is part of their duty to educate any one who is interested. They have had visitors from Spain, Africa, South America, Australia and other countries.

DR. HENRY D. CHAPIN, New York: I wish to thank those who have taken part in the discussion for their remarks.

THE CARTOONIST AND CHILD BEHAVIOR. DR. JOHN RUHRÄH, Baltimore.

This presentation consisted in the exhibition of a series of lantern slides demonstrating the following topics: the upbringing of children by the Aztecs, including the regulation of their food, their punishment for disobedience by thorns and whipping and for lying by exposure while tied, and night labor, as well as their vocational training. It was also shown that in Germany before Columbus' time the birch was the symbol of the school, and that care in feeding was a major consideration.

The tendency in modern times to remove restrictions on the child's self-expression was noted. The increase in the feeding problem due to the stress on the amounts of food is brought out, and slides were shown to support the idea that the increase in the number of problem children at present is due to the psychologic methods used in investigating child behavior. Various verses are quoted on this subject. *(To be concluded)*

CHICAGO PEDIATRIC SOCIETY

Regular Meeting, Feb. 20, 1934

CHARLES SCHOTT, M.D., *President*

SCAPHOCEPHALY. DR. CHARLES SCHOTT.

This girl is 3½ years old. I saw her about three days after her birth; at that time her head was as you see it now. All the sutures were wide open in severe hydrocephalus, except the sagittal suture, which was tightly closed. I thought at first that the condition was oxycephaly, but evidently it is scaphocephaly.

The child is bright and has been normal, except that at about the age of 9 months she had some ophthalmic symptoms. Dr. Oscar Kraft watched her with me, and he saw some retinal changes at that time, which have now entirely cleared. If one looks at her closely one sees some strabismus, but that comes on only when she is tired, and apparently indicates nothing.

The interesting feature is the head, which does not have the short anteroposterior measurements of oxycephaly, but is long in the anteroposterior direction. Looking at the patient from the front when her bonnet is on, one would not notice anything wrong, but from the side the condition is evident. The contour of the head has not changed since she was 9 months of age.

I have never seen a similar case. Children with this condition are not supposed to have any lesions of the central nervous system, and this child is normal in all ways except in regard to the shape of the head. Roentgenograms taken at the age of a few months showed nothing wrong, except that the sagittal suture was entirely closed. Oxycephaly is supposed to have a hereditary background, but scaphocephaly is accidental and is not accompanied by the serious symptoms that accompany oxycephaly.

ATELECTASIS AND BRONCHIECTASIS IN CHILDREN. DR. WILLIAM E. ANSPACH (by invitation).

This article was published in full in the May 1934 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, p. 1011.

DISCUSSION

DR. JOSEPH BRENNEMANN: This is an extremely valuable paper. I have been much interested in all that Dr. Anspach has discussed. His work throws light on a rather murky subject and coordinates several points in an instructive manner. In sorting out some of the old roentgenograms of the Children's Memorial Hospital Dr. Anspach recently looked over about 15,000 films. Among these he found about 100 showing triangular shadows, of which 50 are reported on in his paper. Many of the patients concerned have been under constant observation; others were brought in by the social service workers, in one instance after an interval of twelve years. In at least six instances there have been confirmatory autopsies. In one case there were two triangular shadows; one disappeared, and the condition indicated by the other developed into typical bronchiectasis. Physicians are all familiar with the clinical picture of a collapsed lung or acquired atelectasis, probably chiefly in connection with foreign bodies impacted in the bronchi, when the sequence is most evident. For years physicians have seen these triangular shadows and wondered what they meant. The current explanation never appealed to me, especially the idea that they were mediastinal abscesses. Dr. Anspach's work leaves no doubt in my mind as to what they are.

As for bronchiectasis, probably nearly all the members have had the same experience—one knows little about the pathogenesis, and those whose articles one reads on the subject probably do not know very much more. The value of this paper arises from the fact that it points out a relationship between the triangular shadow, collapsed lung and bronchiectasis, and that it furnishes a rather amazing amount of evidence that there is such a relationship, although it may not cover all the factors that enter into the pathogenesis of bronchiectasis.

There is one point which needs further clarification. It is impossible to tell whether the thick secretions that are regularly found in these conditions act as a plug, causing subsequent absorption of the air and collapse of the lung, or whether there is some primary condition of the lung which causes the thick secretions. In the case of a foreign body, the relationship seems evident. It seems possible that in those cases in which there is not a demonstrable foreign body there is a primary inflammatory condition, possibly atypical pneumonia, which is the primary cause. It makes no special difference, because the therapeutic indication is evidently the same. It seems to me that, in the light of this work, one can carry on the treatment, at least of early bronchiectasis, which probably commonly has its origin in childhood, with renewed enthusiasm. The measures that naturally suggest themselves are the early use of carbon dioxide, bronchoscopic removal of secretions and postural drainage.

DR. ISAAC A. ABT: This interesting paper throws a new light on the origin of bronchiectasis and causes one to wonder whether many of the previously considered cases of congenital bronchiectasis were not acquired, following pulmonary atelectasis.

In every case of bronchiectasis one must presuppose weakness of the bronchial walls, a particular weakness of the muscular layers; the loss of muscular function prevents expiration and favors retention of fluids in the bronchi. The tissues of the bronchial wall may become inflamed and atrophied, the wall may become relaxed, and dilatation of the bronchi may result. In infancy and childhood, fibrosis of the lung following pneumonia or the protracted pneumonias of measles, whooping cough and influenza may lead to bronchiectasis. It should also be noted that bronchiectasis may be associated with diffuse pulmonary tuberculosis.

DR. LOUIS MINSK: I am especially interested in the condition in the new-born. I think that the picture which Dr. Anspach showed in the infant taken six hours after birth is not uncommon. In previous cases I have overlooked it. One knows that the lung expands gradually in the new-born, and not all at once with the first deep breath the baby takes. The expansion may take as long as a month. In that condition roentgenograms will show a rather diffuse haziness of the lung tissue. I wonder if the triangular, uniform, dense shadow which occurs

in a part of a lobe or in an entire lobe may not be due to the aspiration of amniotic fluid. The cases which I have seen shortly after birth have cleared up. Serial roentgenograms have not been taken to show the disappearance of the shadow, but clinically the patients are well. The patient whose roentgenogram Dr. Anspach showed is now entirely well and never had any pulmonary symptoms.

DR. W. E. ANSPACH: In every case of bronchiectasis of a lower lobe in which early roentgenograms have been taken, the triangular shadow has been seen. The process which I have described seems to be a common one. When tuberculosis of the upper lobe exists, a triangular shadow has been an associated finding at the base. The triangular shadow is not specific for any disease; any condition producing occlusion of the bronchi to a lower lobe will produce it. It is rarely found associated with a tuberculous process.

Dr. Minsk's 6 hour old patient was shown because in a recent article the triangular shadow was described as a "shrunken lobe," and the author inferred that the shrinking was due to fibrosis. I wanted to show a case in which the roentgen appearance was like that in the other cases, but in which fibrosis had not had time to develop.

THE RATE OF THE SEDIMENTATION OF ERYTHROCYTES IN RHEUMATIC INFECTION. DR. H. WILLIAM ELGHAMMER.

This article was published in full in the May 1934 issue of the *Archives of Pediatrics*, p. 281.

DISCUSSION

DR. JESSE R. GERSTLEY: This paper is of particular interest to me. Those who were present at the meeting of the Central States Pediatric Society last fall may remember that I presented a clinical study raising the question as to whether chorea is a manifestation of rheumatism. In that paper, representing work done by Dr. Wile, Dr. Falstein, Miss Gayle and myself, we reviewed our material on chorea of the previous eight years. We concluded that there was little evidence, in our cases at least, to suggest that chorea represents a rheumatic process. As there may be two kinds of chorea, one rheumatic and the other nonrheumatic, as suggested in our series of a nonrheumatic origin, Dr. Elghammer's paper not only is of much clinical interest in itself, but is particularly pleasing to us in that it offers experimental corroboration of our clinical findings.

DR. MARK JAMPOLIS: I have observed the clinical application of Dr. Elghammer's work from week to week, and I am convinced that he has opened the way to work that will prove valuable in medical and surgical practice. I believe that this test is one of the best means of determining whether a rheumatic infection is active. I am also convinced that if a child shows a persistently high sedimentation rate, the clinical symptoms must be watched closely, for something serious may be impending. That has been my observation in some of the cases on which Dr. Elghammer did his work.

DR. PHILIP ROSENBLUM: I should like to ask whether the sedimentation findings varied in winter or summer.

DR. I. HARRISON TUMPEER: In one of the curves of the sedimentation rate there were two sharp rises. The first was coincident with high fever and was described as an attack of acute infection of the upper respiratory tract. The second rise, lasting several weeks, was said to be coincident with an acute exacerbation of the endocarditis. There was no demonstrable rise in temperature, although the increased sedimentation rate was as sharp as at the period of the acute infection. Why was there no marked elevation of temperature with acute endocarditis lasting several weeks, and what evidence was there that acute endocarditis existed at this time?

The essayist gave the impression that tonsillectomy generally causes an exacerbation of heart disease because he found that the sedimentation rate increased in several cases. Unless there is some evidence which he has not mentioned, I do

not believe that one can accept the conception of an increased sedimentation rate as being synonymous with an aggravation of the endocarditis.

DR. H. WILLIAM ELGHAMMER: The sedimentation rate seems to be but slightly affected by the seasons. The test should be made at room temperature. I also compared the sedimentation rate taken in the morning with that taken in the afternoon and found no appreciable change in the reading.

As to Dr. Tumpeer's question about the temperature in endocarditis, I think that one should not put too much stress on fever. The general condition of the patient, the pulse rate and, often, findings in the heart determine the diagnosis. In regard to tonsillectomy may I say that one is dealing here with a group of rheumatic children. I had an opportunity to observe several cases of markedly hypertrophic tonsils without any demonstrable infection. Tonsillectomy was performed in these cases, and an increase in the sedimentation rate following the operation was not found.

CONGENITAL DEFECTS OF THE HEART. DR. STANLEY GIBSON.

The most frequent congenital cardiac anomalies are defect of the interventricular or of the interauricular septum and open ductus arteriosus. When any of these lesions exists in pure form, arterial blood is shunted into the venous circuit, as the pressure on the left side of the heart is normally higher than that on the right. If, however, owing to a pathologic condition in the lungs or to the presence of associated defects in the heart itself, the pressure on the right side of the heart exceeds that on the left, a flow in the opposite direction occurs, and venous blood mingles with the arterial stream. It has been shown that this mixture of venous blood with arterial blood is the essential factor in the production of the cyanosis of congenital heart disease.

Among the defects which result in arterial-venous shunt, defect of the interventricular septum and open ductus arteriosus present fairly typical signs which enable one to make a diagnosis ante mortem with some confidence. With defect of the interventricular septum, the patient appears well and the heart is not much enlarged, but a harsh systolic murmur is heard, its point of maximum intensity being in the third or fourth interspace on the left. A thrill is present in a fair proportion of the cases.

With open ductus arteriosus, the heart may be normal in size or slightly enlarged, and dilatation of the pulmonary artery may be sufficient to yield an area of dulness on percussion in the first and second interspaces on the left or may show a characteristic shadow on the roentgenogram. The pathognomonic sign is a continuous harsh machine-like murmur over the precordium, usually maximum in the first and second interspaces on the left and widely heard. It is frequently accompanied by a thrill.

Defects which result in venous-arterial shunt are likely to be multiple and complex, and the handicap to the circulation may be so great that life can be maintained for only a short time. Diagnosis of the anatomic lesions is difficult or impossible. There is, however, one combination which occurs frequently in the cyanotic group known as the tetrad of Fallot. This consists of pulmonary stenosis, defect of the interventricular septum, dextroposition of the aorta and hypertrophy of the right ventricle. This condition is compatible with a fairly long life, though the majority of the patients succumb in childhood. The symptoms are breathlessness and cyanosis with its attendant phenomena. The heart is enlarged in its transverse diameter and shows a characteristic roentgenographic shadow, the so-called boot-shaped heart, which is due to hypertrophy of the right ventricle. The picture is completed by a harsh systolic murmur in the second interspace on the left, with or without a thrill.

In addition to the cases of arterial-venous and venous-arterial shunts there is a third group of congenital cardiac anomalies which are not featured by any abnormal communication between the two sides of the heart, but which may throw an extra load on the heart or furnish a point of lowered resistance to the invasion

of bacteria. In this group coarctation of the aorta is perhaps the most important lesion. It consists of a narrowing of the aorta in the region of the ductus arteriosus. If the coarctation is of high grade, a collateral circulation must be established to supply the lower part of the body. This results in dilatation of the intercostal arteries, which may be palpable as throbbing masses in the interscapular region, beneath the axillae or over the front of the chest. The blood pressure is elevated in the arms, while it is low or unobtainable in the legs. Palpation over the femoral artery discloses feeble pulsation or absence of pulsation. A murmur over the aortic area is frequently present.

While the obscurity and complexity of the lesions of congenital heart disease render accurate diagnosis impossible in many instances, increasing study of the detailed symptoms and signs, with special emphasis on roentgenologic findings, has served to bring about greater precision in diagnosis in this difficult field.

The prognosis varies widely, depending on the nature of the lesion. With anomalies which throw little additional burden on the circulation ripe old age may be attained. On the other hand, the handicap may be so extreme that death in early infancy results.

A further element of danger which is not sufficiently appreciated is the frequent occurrence of complicating bacterial endocarditis. In Abbott's series of cases this complication occurred in practically 20 per cent. Because of this fact the prognosis should always be guarded.

Treatment is directed toward proper supervision of the patient's activities and avoidance of infection.

DISCUSSION

DR. ISAAC A. ABT: An exact clinical diagnosis of congenital heart disease presents difficulties, and one who hazards such a diagnosis is frequently disappointed by the observations at autopsy. Dr. Gibson referred to the classic paper of Dr. Maude Abbott in Osler's "Modern Medicine," and when one recalls all the malformations and lesions which Dr. Abbott records, one is reminded of the classifications of Linnaeus or Cuvier. It is amazing how many malformations may occur, either singly or in combination. Time did not permit Dr. Gibson to refer to all the cardiac lesions which might occur in early life, but one sometimes finds inflammatory lesions in the new-born, particularly when mothers have suffered from an infectious disease during pregnancy.

During the last epidemic of influenza a mother who was ill with this disease gave birth to an infant who died during the first days of life; at autopsy the infant showed acute infectious endocarditis.

Attention has also been called to the most infrequent occurrence of infective myocarditis in the new-born. Dr. Feller of the Pathological Institute in Vienna has described a number of such cases.

It has also been suggested that some of the so-called idiopathic cardiac hypertrophies occurring in early life may be the result of persistent infectious myocarditis.

DR. JOSEPH BRENNEMANN: At autopsy in patients with congenital cardiac conditions of the more serious type one observes so many unexpected and complicated combinations that it rather discourages attempts to make an accurate diagnosis ante mortem in such cases.

As for congenital idiopathic hypertrophy of the heart, I have always believed that "idiopathic" meant even less than it usually does in cases of that sort. The thought always suggests itself that there is some condition which throws an extra amount of work on the heart or some peculiar condition that increases the bulk of the heart without reference to muscular hypertrophy. Physicians know now that there is a type of cardiac enlargement without valvular involvement or obstruction that is due to interstitial myocarditis. They also know that there is a type of congenital enlargement in which the much greater size of the heart is due to the storage of glycogen. I recently saw a heart of this type which was different from any I had ever seen. The walls were enormously thickened and almost pearly

gray. On hearing that Dr. Kato and Dr. Humphries were reporting a case of idiopathic hypertrophy due to the storage of glycogen, I immediately sent for the heart, which I had seen in a neighboring city, feeling sure that it belonged in this category, and it did. Dr. Kato has since seen two other cases of this type.

DR. JESSE R. GERSTLEY: In my experience, the most severe types of congenital lesion are often unaccompanied by a murmur. One hears a pistol shot tone but no murmur. I should like to know whether that has been Dr. Gibson's experience.

DR. JAMES H. WALLACE: The only point that I might emphasize is the expectancy of life in these cases, which, I think, is less than one is inclined to believe. When one hears a congenital murmur in a child's heart and the heart function seems normal, it is a common practice to say that it means little, and yet, as Dr. Gibson emphasized, Abbott has shown that the expectancy of life in congenital heart disease, as a whole, is decidedly decreased. It is the habit to treat these signs rather lightly. I used to wonder why insurance companies are inclined to impose higher rates for any one who has a murmur, regardless of its cause, but when one considers that a certain percentage of these murmurs signify a congenital lesion this attitude is more readily understood.

DR. H. G. PONCHER: Recently, at the Research and Educational Hospital of the University of Illinois we collected two instances of an anomalous coronary artery coming from the pulmonary artery and supplying the left ventricle with venous blood. In both these cases the left side of the heart was markedly hypertrophied. In some cases of this kind glycogen has been found, but I doubt whether the storage of glycogen is responsible for the hypertrophy. There are not many cases of this type reported in the literature. I wonder whether the anomaly of the coronary artery has been adequately considered in hypertrophy of the heart without apparent cause in infants.

DR. W. L. CRAWFORD, Rockford, Ill.: Since Dr. Brennemann and Dr. Poncher both mentioned the cases of glycosuria, I think it may be worth while to report probably the only case recorded in a twin which was due to defective storage of glycogen. I saw the patient's twin within a week or two, and it is apparently normal and healthy.

DR. STANLEY GIBSON: Dr. Abt is right in stating that many patients with congenital heart disease show surprising conditions at autopsy, diagnosis of which is impossible during life. What I have attempted to do is to point out that there are a certain number of conditions which do allow a fairly accurate clinical diagnosis. Moreover, an appreciation of the possibilities in cases of multiple and complex lesions in which cyanosis is present is worth while.

Concerning Dr. Gerstley's question relative to the absence of murmurs in congenital heart disease, my experience is that absence is relatively rare. However, one can readily appreciate that a transposition of the blood vessels or an absence of the cardiac septums might fail to produce a murmur and yet produce serious symptoms.

Book Reviews

Les pleurésies à pneumocoques dans l'enfance. By M. Péhu and A.-Z. Rougier. Price, 30 francs. Pp. 173, with 27 illustrations. Paris: Gauthier-Villars & Cie, 1934.

This monograph deals with the clinical aspects of pneumococcic pleuritis of various types in infants. The first chapter covers the history of the development of the scientific knowledge of pleurisy. The etiology of pleurisy is discussed in relation to the bacteriology of the pneumococcus, portals of entry, time of appearance, frequency and influence of age and season. The pathologic anatomy is thoroughly discussed. About two thirds of the treatise is devoted to the symptoms, complications, diagnosis, prognosis and treatment of pneumococcic pleuritis. There are twenty-seven reproductions of illustrative roentgenograms. The emphasis throughout is on the practical and clinical aspects, which are presented in great detail.

Die akuten Infektionskrankheiten des Kindesalters. By Dr. Egon Helmreich. Price, 4.80 marks. Pp. 140. Berlin: Julius Springer, 1934.

It is rare to find in so concise a form such a complete and satisfactory discussion of the infectious diseases of childhood. The presentation of the material gives evidence of the author's wide experience and sound judgment. The diseases considered are: diphtheria, scarlet fever, measles, rubeola, the fourth disease (Dukes-Filatow), erythema infectiosum, exanthema subitum, chickenpox, smallpox, aphthous stomatitis, mumps, whooping cough, poliomyelitis, epidemic meningitis, tetanus neonatorum, erysipelas, typhoid and paratyphoid fever and the infectious diarrheas.

Two tables are included, one giving incubation periods and methods of transmission, and the other giving statistics of notifiable diseases in European countries and the United States.

The Life of Sir Robert Jones. By Frederick Watson. Price, $3.75. Pp. 327, with 10 illustrations. Baltimore: William Wood & Company.

This delightful biography of the most eminent of British orthopedic surgeons is written by his son-in-law. It depicts the life of a man who made an eminent success without much of an early struggle. Sir Robert Jones was a great organizer and a great humanitarian, as well as a great orthopedic surgeon. He was fortunate in that his gifts and experience were at their full maturity when they were most needed, that is, at the time of the World War. The book gives the impression of a man not only great in work, but thoroughly enjoying life. It is not a critical biography, but a narrative one.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. A. Graeme Mitchell, Children's Hospital, Cincinnati.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Atlantic City, N. J. Time: June 10-14, 1935.

American Academy of Pediatrics

President: Dr. Thomas B. Cooley, 1728 Seminole Ave., Detroit.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: New York. Time: June 7-8, 1935.
Region I. Place: New York, Ambassador Hotel. Time: Oct. 19-20, 1934.
Region II. Place: San Antonio, Texas. Time: Nov. 14, 1934.
Region III. Place: Rochester, Minn. Time: Oct. 4, 1934. Place: Minneapolis. Time: Oct. 5-6, 1934.
Region IV. Place: Oakland, Calif. Time: November 1934.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st., New York.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.
Place: Philadelphia. Time: Sept. 24-28, 1934.

American Pediatric Society

President: Dr. Borden S. Veeder, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.

Canadian Society for the Study of Diseases of Children

President: Dr. D. P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary-Treasurer: Dr. R. R. Struthers, 1414 Drummond St., Montreal.
Place: Buffalo, N. Y. Time: June 1935.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Joseph Stokes Jr., Children's Hospital, Philadelphia.
Secretary: Dr. A. A. Weech, Babies Hospital, New York.
Place: Atlantic City, N. J. Time: May 1935.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Arthur H. Gray, 1117 Second Ave., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Oliver W. Hill, 511 W. Church St., Knoxville, Tenn.
Secretary: Dr. Madison Hines Roberts, 104 Ponce de Leon Ave., N. E., Atlanta, Ga.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Benjamin Bashinski, 700 Spring St., Macon.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta. Time: Oct. 25, 1934; May 1935.

Louisiana State Pediatric Society

President: Dr. John Signorelli, Louisiana State University Medical School, New Orleans.
Secretary-Treasurer: Dr. Edwin A. Socola, Louisiana State University Medical School, New Orleans.
Place: New Orleans. Time: April 1935.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. W. A. Collins, 103 W. Burdick St., Kalamazoo.
Secretary: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.

Mississippi State Pediatric Society

President: Dr. N. C. Womack, Jackson Infirmary, Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 725 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. Fifth St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. Seventh St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. C. V. Rice, 222 Wall St., Muskogee.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.
Place: Oklahoma City. Time: May 1935.

South Carolina Pediatric Society

President: Dr. Julian P. Price, Medical Bldg., Florence.
Secretary-Treasurer: Dr. Leland B. Salters, 317 S. Warley Ave., Florence.

Tennessee State Pediatric Society

President: Dr. Arthur G. Jacobs, 1193 Madison Ave., Memphis.
Secretary: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.

Virginia Pediatric Society

President: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.
Secretary: Dr. W. A. McGee, 2618 Grove Ave., Richmond.
Place: Alexandria. Time: Oct. 9-11, 1934.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry M. Greenwald, 499 Ocean Ave., Brooklyn.
Secretary: Dr. Sylvan D. Lazarus, 847 Lincoln Place, Brooklyn.
Place: Medical Society of County of Kings Bldg., 1313 Bedford Ave., Brooklyn.
Time: Third Wednesday of each month from October to May, 8:30 p. m.

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. A. Garvin, Carnegie Medical Bldg., Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Morris Gleich, 9 Post Ave., New York.
Secretary: Dr. Harry D. Pasachoff, 1560 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Earl W. May, 1551 Woodward Ave., Detroit.
Secretary: Dr. Edward A. Wishropp, 5057 Woodward Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Muse, 384 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Frank Lancaster, Medical Arts Bldg., Houston, Texas.
Secretary-Treasurer: Dr. A. A. Little Jr., 817 Holman Ave., Houston, Texas.
Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Henry A. Reisman, 148, 88th Ave., Jamaica, L. I.
Secretary-Treasurer: Dr. Edith A. Mittell, 112 Queens Blvd., Forest Hills, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Clyde V. Croswell, 1052 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. F. R. Janney, 1411 Wauwatosa Ave., Wauwatosa, Wis.
Secretary: Dr. John H. Reynolds, 1628 Wisconsin Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. James L. Gamble, 33 Edgehill Road, Brookline, Mass.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S. Minneapolis.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala, Pa.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

RICHMOND PEDIATRIC SOCIETY

President: Dr. W. A. McGee, 2618 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Emily Gardner, 1100 W. Franklin St., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

ROCHESTER PEDIATRIC SOCIETY

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Secretary: Dr. Ralph Verploeg, 19th and Gilpin Sts., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Armin C. Rembe, 1215 4th Ave., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place, College Club. Time. Third Friday of each month, 7 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Victor E. Stork, 1136 W. Sixth St., Los Angeles.
Secretary: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. John F. Sanders, 320 Townsend St., Lansing, Mich.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Nov. 23-24, 1934.